V.

EXPOSURE TO ENVIRONMENTAL TOBACCO SMOKE

The purpose of this chapter is to examine the available information on exposure to ETS, and to estimate exposures of various subgroups of the California population to ETS.

Information from Chapter 2 (*Exposure Measurement and Prevalence)* of the 1997 Cal/EPA report: *Health Effects of Exposure to Environmental Tobacco Smoke* was used as a starting point for the development of this chapter. Literature published subsequent to that report was then reviewed and is summarized in this section. This chapter includes a discussion of ETS exposure prevalence in California; a discussion of markers or surrogates used by researchers to estimate air concentrations of ETS; a review of measured and modeled air concentration studies on the constituents of ETS; and the results of ARB's recent ETS air monitoring study. This chapter also presents scenario-based estimates of selected population subgroups' exposures to ETS under different smoking conditions and includes an assessment of children's exposures to ETS as required pursuant to the State's adoption in 1999 of the Children's Environmental Health Protection Act (Senate Bill 25, Escutia). An assessment of the contribution of indoor exposure to total exposure is also presented in this chapter, as required by Health and Safety Code Sections 39660 and 39660.5.

In Part B of this report, which describes the health effects of ETS, OEHHA estimates a range of ETS-related health effects for the California population. The range of estimated health effects is based on today's levels of ETS exposure for all members of the public and represents a range, which corresponds to the range of exposures that are present throughout the State. This report reflects the range of exposures that may be found throughout the State.

A scenario-based approach was used to characterize the range of the public's exposure to ETS in this report. The scenario-based exposure method uses the results from ARB's ETS air monitoring study, available indoor ETS concentration data, and scenario-based activity patterns to estimate exposures under different conditions. This approach differs from previous TAC exposure assessments, which were based on California population-weighted exposures to outdoor average ambient concentrations. That approach was appropriate for TACs emitted from area-wide or region-wide sources such as motor vehicles and industrial plants. However, cigarettes and cigars, the primary sources of ETS, are smaller sources that emit pollutants near people, and ETS is not monitored at ambient monitoring stations. Therefore, because ETS emissions and exposure are very localized, and because only very limited data on outdoor ETS levels are available, we believe the scenario-based approach provides better and more informative estimates of public exposure to ETS.

A. CALIFORNIA ACTIVITY PATTERNS AND ETS EXPOSURE

An individual's exposure is equally dependent on the air concentration of a pollutant in a given environment, and the time they spend in that environment. An individual's total daily exposure is the sum of the many exposures they experience across their 24-hour day, including both indoor and outdoor environments. Thus, exposure may be heavily influenced by an individual's activity patterns if they routinely visit a location where smoking occurs, or if they live in a smoking household.

Californians (over 11 years old) spend an average of about 87% of their time indoors. National and California surveys show that children and adolescents spend a majority of their day indoors, especially at home (Phillips *et al*., 1991; Jenkins *et al*., 1992; Klepeis *et al*., 2001a). As shown in Table V-1 below, California adults (over 11 years old) spend about 62% of their time in their home, and children under 12 years of age spend about 76% of their time in the home, on average. Thus, if smoking occurs in an individual's home, exposure in the home typically contributes the major portion of that individual's exposure to ETS.

Table V-1

Percent of Time Californians Spend in Major Locations

AGE	PERCENT OF TIME			
	Inside the Home	Other Indoors	Outdoors	Inside a Vehicle
Children[1]				
0 – 2	85	4	7	4
3 – 5	76	9	10	5
6 – 11	71	12	13	4
All Children (0 - 11)	76	10	10	4
I. Teens 12-17	61	27	6	6
II. Adults 18 +	62	25	6	7
III. All Adults and Teens[2]	62	25	6	7

[1]From: *Study of Children's Activity Patterns*, Wiley *et al.*, 1991a, ARB Contract no. A733-149; Phillips *et al*., 1991).
[2]From: *Activity Patterns of California Residents*, Wiley *et al.*, 1991b, ARB Contract no. A6-177-33; Jenkins *et al*., 1992).

Implementation of smoking restrictions at the workplace and public places in California has greatly reduced the overall exposure of non-smokers to ETS. Other non-smokers exposure occurs in many locations, such as at bus stops; entrances to office buildings where smokers congregate; parking lots; outdoor sporting events; outside of airport

terminals; and inside homes of people who smoke. Children with smoking parents generally experience high exposures to ETS due to their proximity to their parents, with the highest exposures typically being inside homes and vehicles. Teens, college students, and elderly individuals may also experience high exposures due to activities with smoking peers and/or roommates or home residents who smoke. However, older children and some adults spend a substantial portion of their non-sleeping time outdoors. For those individuals, outdoor exposure to ETS may predominate, and may be substantial.

As discussed in the next section, data on smoking prevalence and time non-smokers are near smokers indicate that both smoking rates and the exposure of non-smokers are declining in California. By 1999, 37% of non-smoking Californians reported that they had not been near a smoker in the past six months (Gilpin *et al*., 2001). Gilpin *et al*. (2001) also reports that in 1999, 88% of children and adolescents lived in smokefree homes. These findings and the data in Section C below on indoor concentrations in smoking and non-smoking homes suggest that levels of ETS exposure experienced by Californians range from near zero to very high levels.

B. PREVALENCE OF ETS EXPOSURE IN CALIFORNIA

This subchapter presents an overview of the past and present patterns of adults and children's exposure in California. The prevalence studies only represent the time periods covered by the study. Smoking behaviors and other factors that change smoking patterns such as smoking regulations and smoking customs may affect present and future exposure patterns. For this reason, the information presented in this section primarily focuses on the most recent smoking prevalence studies.

Burns and Pierce (1992) conducted the first of a series of California Tobacco Control surveys on tobacco use in California since the passage of the Tobacco Tax and Health Protection Act (Proposition 99) in 1988. The survey covered the period between June 1990 and July 1991 and included a sample population of about 12,000 for children ages 0-5 years; about 13,000 children ages 6-11 years; and, about 12,000 adolescents ages 12-17 years. Smoking prevalence during this time among adult smokers was 22% and adolescents aged 12-17 years was 9.3%. The study also reported that 32% of children under 5 years of age lived in homes with one or more smokers. Similar values were reported for children 6-11 years of age (32%) and adolescents 12 to 17 years of age (37%).

Pierce *et al*. (1994) reviewed the progress of several California Tobacco Control surveys conducted in 1990, 1992, and 1993. Part of the survey included an estimate of the number of women who were exposed to ETS while pregnant. Information from the surveys indicate that the proportion of non-smoking women in California of child-bearing age who are ETS-exposed is estimated to be about 22%. For childhood exposures, the 1993 survey suggests 19.6% of those age 17 and under, and 17.7% of those under age 5 may be exposed to ETS in their homes. Klepeis *et al*. (2001a) compared the data from the National and California surveys for the time children were exposed to a

smoker. The California children study (Jenkins *et al*., 1992) showed that children spent most of their time exposed to ETS in a residence (25% of respondents). Children spent a significant portion of their time exposed to ETS in other locations as well (outdoors-15% and in a vehicle-10%). There were not enough California children respondents in the National Human Activity Pattern Survey (NHAPS) to calculate reliable statistics for the time spent with a smoker in different locations. However, in both studies, the minutes spent per day with a smoker in all locations was close (222 minutes for NHAPS vs 204 for the California children study). The percentage of children who spent time with a smoker was lower in the NHAPS (20%) than the California children study (38%).

Jenkins *et al*. (1992) also estimated the percentage of adults/adolescents who spent time near a smoker. On a given day, adolescent children (ages 12-17) spent an average of 228 minutes of potential exposure in proximity to smokers (adults average 251 minutes). However, a higher percentage of adolescents versus adults reported being near ETS at some time of the day (64% reported yes and 56% of adults reported yes) (Jenkins *et al*. 1992; Miller *et al*., 1998). Table V-2 summarizes the data for time spent near a smoker.

Miller *et al*. (1998) examined exposures of non-smoking Californians (i.e., adults, adolescents, and children) to 17 TACs known to be present in ETS. The investigators used concentration data for a variety of indoor microenvironments in combination with the CARB's activity pattern survey findings to model Californians' ETS exposures for the late 1980s and to make predictions for the late 1990's. The modeling results (for the late 1980s) indicate that of the 62% of adolescents who were exposed to ETS, 62-74% of total exposure was in the home, 8 to 18% occurred while in a vehicle, and 4-15% occurred in retail and other indoor environments (e.g., shopping malls, beauty salons, etc.). For the 33% of children (ages 7-11) exposed to ETS, 70-73% of total exposure was in the home, whereas 9-18% occurred in vehicles and 6-7% occurred in others' homes. The authors' predictions for the late 1990's showed a considerable drop in exposures: 16-19% of adults, 33-35% of adolescents, and 21-23% of children were expected to experience ETS exposure on any given day. Only residences, transportation, and others' residences were examined for the microenvironmental exposure simulations, due to smoking bans in workplaces and public establishments (although non-smokers may be exposed to ETS in public establishments that still allow smoking (Weber *et al*., 2003)). The results predicted that one's own home would be the major site of exposure for all age groups: 58-69% for adults, 58-66% for adolescents, and 72-83% for children.

In a study by Gilpin *et al*. (2001), adolescent (12-17 years) smoking prevalence increased between 1993 (9%) and 1996 (12%), but by 1999 had fallen to about 8%, lower than the prevalence in 1990 (9%). An increase in smokefree homes has resulted in lower exposure to ETS in the home. In 1999, 88.6% of children and adolescents lived in smokefree homes, up from 77% in 1993. The report also suggests that parental reinforcement of strong expectations against smoking for their adolescent youth is strongly associated with low rates (11.7% overall) of adolescent smoking and is likely a key parenting practice to deter adolescent smoking throughout adolescence into adulthood.

Table V-2

Prevalence of ETS Exposure in California

Population	Percent of Non-smokers Reporting ETS Exposures	Reported Average Daily ETS Exposure Duration (minutes)	Reference
Adults	56%	251	Jenkins *et al*., 1992 Miller et al., 1998
Adolescents (12-17)	64% 33-35%	228 NA	Jenkins *et al*., 1992 Miller *et al*., 1998
Children (0-11)	38% 20% 21-23%	204 222 NA	Wiley *et al*., 1991b Klepeis *et al*., 2001a Miller *et al*., 1998

C. MONITORING FOR ETS

Tobacco smoke is composed of several thousand individual compounds (Dube and Green, 1982). Pyrolysis, pyrosynthesis, and distillation lead to the formation and emission of these compounds as a mixture in environmental tobacco smoke (Ogden and Jenkins, 1999). Since tobacco smoke is a complex mixture, it cannot be measured directly. Given the complex nature of ETS, it is necessary to select a surrogate measure of exposure that are representative of ETS as a whole. Other methods include source apportionment and modeled emissions.

1. ETS Markers

In 1986, the National Research Council listed attributes for an ideal surrogate or marker for ETS (NRC, 1986). These include uniqueness, ease of measurement, similar emission rate when compared with a variety of ETS constituents, and consistent behavior under a range of environmental conditions. No single ETS component meets all of the attributes of an ideal marker.

Several components of ETS have been studied as markers for ETS. Nicotine has been most widely studied as a potential marker because its only source is tobacco smoke (Hammond *et al.,* 1987). Nicotine has been used as a pesticide, but only in very limited locations and applications. Sampling and analysis methods are well documented for nicotine, as demonstrated by several authors. Ninety-seven percent of indoor air nicotine has been found in the vapor phase (Ogden and Jenkins, 1999). Adsorption by nicotine on indoor surfaces complicates indoor air measurements. Adsorption should be less of a concern for outdoor measurements near sources of ETS. Other ETS markers that have been studied include: solanesol, 3-ethenylpyridine (3-EP), carbon monoxide, iso- and anteisoalkanes (C_{29}-C_{34}), PAHs, fluorescing particulate matter, respirable suspended particles (RSP), and ultraviolet particulate matter (Ogden and Jenkins, 1999; Rogge *et al*., 1994). Solanesol, a semivolatile compound adsorbed to

particulate matter, has been used as a marker for particulate matter from ETS in indoor air (Daisey, 1999). However, solanesol is thought to degrade when exposed to ultraviolet light and hence, would not be a good marker for ETS outdoors. Also, solanesol air concentrations may be too low to measure (Jenkins *et al*., 2000) and does not have a steady correlation with RSP levels nor is it consistent across different tobacco products (LaKind *et al*., 1999). 3-EP is better than nicotine as a marker for vapor phase ETS (Jenkins *et al*., 2000). However, analytical standards for 3-EP are not as readily available as for nicotine (Poore, 2002). Carbon monoxide readily dilutes to near background concentrations away from the source of the ETS (Jenkins *et al*., 2000). Fluorescing, respirable, and ultraviolet particulate matter are not as unique to tobacco smoke as nicotine, solanesol, or 3-EP (Ogden and Jenkins, 1999). Finally, iso- and anteiosoalkanes may be more stable as tracers in the outdoor urban atmosphere. Iso- and anteiosoalkanes are enriched in cigarette smoke particles and show a concentration pattern characteristic of tobacco leaf surface waxes.

Although several indicators have been determined as markers for ETS, particles and nicotine have been used most widely. Whereas there are many sources of particles in the air with varying background exposures, nicotine is specific to smoking and thus makes a good marker for ETS. Consequently, the ARB study focuses on nicotine as a marker for ETS concentrations and exposures.

2. Ambient Air Monitoring Studies for ETS

Several compounds or groups of compounds have been used to measure ETS in the ambient air. One study by Rogge *et al*. (1994) estimated concentrations of fine cigarette smoke particles in the Los Angeles outdoor air based on measurements of iso- and anteisoalkanes from data taken in 1982. These compounds are associated with tobacco leaf waxes and are preserved in the atmosphere on the cigarette smoke particles. Using these marker compounds, ambient fine cigarette smoke particles are estimated to be present at a concentration of 0.28 to 0.36 $\mu g/m^3$ in outdoor Los Angeles air, accounting for 1.0% to 1.3% of the fine particle mass concentration.

Jenkins *et al.* (1996) conducted personal air sampling in 16 U.S. cities, including Fresno. The monitoring included home and workplace environments with and without exposure to ETS. Monitoring was conducted for eight ETS markers. As found in other studies, homes were found to pose the highest ETS exposure, for those who lived or worked in smoking environments. These data are presented later in this chapter in the indoor air concentrations of ETS section.

In another California study, Eisner *et al*. (2001) used passive badge monitors to measure personal exposures to ambient nicotine. In this study, fifty adult asthmatics were chosen based on their reported ETS exposures or potential exposures from a survey administered from an existing asthma cohort study. Each of the study participants wore passive badge nicotine monitors over a 7-day test period and reported ETS exposures in six selected microenvironments (participant's home, another persons home, in-vehicle, workplace, bars/nightclubs, and outdoor locations). The collected nicotine was analyzed by gas chromotography with nitrogen selective detection. The

nicotine concentrations were calculated by dividing the total nicotine collected, over the monitoring period, by the estimated volume of air sampled. The results show that the overall median 7-day nicotine concentration was reported to be 0.03 $\mu g/m^3$ in all microenvironments. Measured median nicotine concentrations were highest among persons who reported ETS exposures at home (0.61 $\mu g/m^3$), work (0.03 $\mu g/m^3$), and in other (outdoor) environments (0.025 $\mu g/m^3$).

3. ARB's Ambient ETS Monitoring Study

The ARB staff conducted ambient air monitoring at outdoor smoking areas for nicotine as part of the ARB's evaluation of ETS as a potential toxic air contaminant. This study was undertaken to provide data to fill in the gaps that existed in outdoor measurements of ETS. Nicotine was used as a surrogate for ETS based on the reasons given previously regarding ETS surrogates. The purpose of this monitoring was to measure air concentrations of nicotine at different locations in California and for different durations (1-8 hours). The locations were selected based on potential public ETS exposures. These concentrations were then used to estimate outdoor near-source public exposures to ETS in locations representing several exposure group sub-populations. We used the mean and highest measured concentration from the sites tested to estimate a persons potential mean and high end exposure to ETS. This was done to show that some Californians may be exposed to levels generally associated with indoor ETS concentrations.

Monitoring was conducted during 2003 at outdoor smoking areas at the following five locations: an airport, junior college campus, public building, office complex, and amusement park. A site was chosen in Sacramento as an initial test location to verify that there were no problems with the sampling and analysis methods. No problems were found. The remainder of the monitoring was conducted in southern California.

The California Department of Health Services distributes funds to counties for anti-smoking education programs. Staff in the County Health Departments in Los Angeles and Ventura Counties expressed interest to the ARB in having monitoring conducted in their counties. These two county departments provided funding to the ARB to cover monitoring expenses, in return for ARB conducting ETS monitoring in their counties.

At each of the study sites, sampling was conducted for nicotine over a three-day time period during typical business hours (between 8:00 am and 5:00 pm). Two of the days were devoted to 8-hour samples; six one-hour samples were collected on one of the sampling days. For each sampling period, two samplers were situated adjacent to the outdoor smoking area, with a third sampler located away from the smoking area as a background sampler in the expected upwind direction. Several methods have been used for collecting air samples of nicotine (Caka *et al.*, 1990). During this monitoring, nicotine was collected on XAD-4 adsorbent resin by pulling air through sampling cartridges at a rate of 15 liters per minute. The sampling cartridges contained about 30 milliliters of XAD-4 resin. Analysis was conducted by gas chromatography with a mass selective detector. The estimated quantitation limit (EQL) was 0.029 $\mu g/m^3$ for the 1-

hour samples and 0.0036 $\mu g/m^3$ for the 8-hour samples. Concentrations measured below the EQLs were reported as trace.

The ARB staff collected meteorological data including wind speed/direction and ambient temperatures at three of the study sites. We did not collect meteorological data at two of the study sites due to the physical obstacles and variable wind patterns that existed at these sites.

In addition, the ARB staff counted the number of cigarettes smoked during each sampling period to determine the subsequent exposures. A summary of the monitoring results is presented in Table V-3. Overall, the results indicate that concentrations of nicotine correspond to the number of smokers in the smoking areas, although factors such as the size of the smoking area and wind speed affected the results, as illustrated by the range in results at individual study sites and between study sites. A complete description of the monitoring and results is contained in Appendix C**.**

Quality assurance samples (trip and field blanks, trip and field spikes, and collocated samples) were also collected. No nicotine was detected in the trip blanks. Some field blanks contained trace levels of nicotine, but all field blanks were below the EQLs. Trip spikes had recoveries that ranged from 72-89 percent. Field spikes had recoveries that ranged from 76-87 percent. There were two 8-hour and two 1-hour collocated sampling periods with quantifiable levels of nicotine. The comparison of collocated samples (calculated as the difference between the two collocated samples divided by the mean of the two samples) ranged from 32-58 percent for the 8-hour samples and was 42-54 percent for the 1-hour samples.

The results of the monitoring study show a wide range of exposures depending on the locations and number of cigarettes smoked. Mean 8-hour concentrations ranged from 0.013 (local government center) to 3.1 $\mu g/m^3$ (amusement park). Mean 8-hour background concentrations ranged from 0.009 (junior college) to 0.12 $\mu g/m^3$ (amusement park). It is important to note that the background concentrations measured in this study may not be representative of background nicotine levels throughout southern California. At most sites, the location of the background monitors, due to physical obstacles and/or meterological conditions, were close to the smoking areas (see Appendix C for more detail and location of sampling sites). However, even at the background site locations, background concentrations were substantially lower than measured in the smoking areas. Mean 1-hour concentrations ranged from less than the EQL (0.029 $\mu g/m^3$ for 1-hr) (junior college and local government center) to 0.17 $\mu g/m^3$ (amusement park).

Table V-3

Results of ARB Nicotine Air Monitoring Adjacent to Outdoor Smoking Areas

Site Tested	8-hour Data	Concentration ($\mu g/m^3$)	Cigarettes Smoked (8 hours)		1-hour Data	Concentration ($\mu g/m^3$) [b]	Cigarettes Smoked (1 hour)
Airport	Mean Day 1 [a] Mean Day 2 [a] 2-Day Mean Range Mean bkgd.	0.61 0.74 0.68 0.48 - 0.99 0.021	261 326 294		Maximum Mean Range Mean bkgd.	1.5 0.72 0.36 - 1.5 0.046	61 75
Junior College [c]	Mean Day 1 Mean Day 2 2-Day Mean Range Mean bkgd.	0.035 0.018 0.027 0.013 – 0.044 0.012	30 34 32		Maximum Mean Range Mean bkgd.	0.15 0.051 0.017 - 0.15 <EQL [d]	5 4
Local Govern-ment Center [c]	Mean Day 1 Mean Day 2 2-Day Mean Range Mean bkgd.	0.066 0.055 0.061 0.042 – 0.073 0.009	59 60 60		Maximum Mean Range Mean bkgd.	0.18 0.097 0.039 - 0.18 <EQL	15 11
Office Complex [c]	Mean Day 1 Mean Day 2 2-Day Mean Range Mean bkgd.	0.12 0.14 0.13 0.11 - 0.15 0.09	261 251 256		Maximum Mean Range Mean bkgd.	0.28 0.19 0.10 - 0.28 0.06	31 29
Amuse-ment Park	Mean Day 1 Mean Day 2 2-Day Mean Range Mean bkgd.	2.6 2.8 2.7 2.4 - 3.1 0.12	653 719 686		Maximum Mean Range Mean bkgd.	4.6 2.4 0.66 - 4.6 0.17	148 91

[a] Mean concentration of samples adjacent to outdoor smoking area.
[b] Maximum, mean, range, and mean background concentration of six 1-hour sampling periods. (Means include all samples, with trace values below the EQL assigned 0.017, the midpoint between the EQL and limit of detection.)
[c] Light to moderate winds all three days of monitoring at this location.
[d] EQL for 1-hour samples of 0.029 $\mu g/m^3$; EQL for 8-hour samples of 0.0036 $\mu g/m^3$ (1 $\mu g/m^3$ of nicotine = 0.15 ppbv).

4. Modeled Ambient Concentrations for ETS

Schauer *et al*. (1996) used a chemical mass balance (CMB) receptor model based on organic compounds to estimate source contributions to airborne fine particle mass concentrations in the Los Angeles air. Receptor-based CMB models use emission source chemical composition profiles to linearly extrapolate source contributions to the measured chemical composition of ambient samples (Watson, 1984). The model was applied to four air quality sites in southern California using atmospheric organic compound concentration data and source emission profile data collected specifically for the purpose of testing this model (Gray *et al*., 1986, Hildemann *et al*., 1991; Rogge *et.*

al., 1993). The contributions to fine organic aerosol of up to nine primary particle source types were identified: diesel engine exhaust, paved road dust, gasoline-powered vehicle exhaust, emissions from food cooking and wood smoke, with smaller contributions from tire dust, plant fragments, natural gas combustion aerosol, and cigarette smoke. Using the fine organic aerosol concentration data and source emission profile data, Schauer *et al*. (1996) estimated annual average ETS fine particle mass concentrations of 0.21 μg/m^3 in the Los Angeles area (average of the four sites studied). Table V-4 summarizes the results from outdoor measurement or modeled studies on the constituents of ETS.

5. Estimated Los Angeles Outdoor Annual Average Ambient ETS Air Concentrations

Although a scenario-based approach was used to characterize the range of the public's exposure to ETS in this report, Californians who neither smoke nor associate with many smokers will have limited ETS exposure. In this case, individuals will likely experience the majority of their lifetime ETS exposure from background levels of ETS which results from the contribution of occasional or steady state near-source emissions. Since most Californians live and work in urban areas, it would be helpful to ascertain what outdoor ambient ETS levels could exist in these areas. For comparison purposes only, the ARB staff estimated an outdoor annual average ambient ETS fine particle concentration for the Los Angeles area for 2003.

This estimate is derived from data collected from studies done by Schauer *et al*., 1996 and Rogge *et al*., 1994. As discussed in previous sections of Chapter V, these studies estimated annual average ETS fine particle concentrations in the Los Angeles air based on 1982 data. To calculate a 2003 Los Angeles annual average ETS fine particulate concentration, staff applied an adjustment factor to the 1982 fine PM estimates presented in the Schauer *et al*. (1996) and Rogge *et al*. (1994) studies to reflect reductions in cigarette sales and cigarette emission rates since 1982. We used current cigarette sales data (BOE, 2004) and cigarette emission rate data (Nelson, 1994; Nelson *et al*., 1997; Martin *et al.,* 1997; Repace, 2001) for these calculations. The analysis is premised on the assumptions that the ratio of fine particle-emitting sources and fine particle ambient concentrations that existed in 1982 are similar to those that exist today. We also assume that the decline in emissions from cigarettes smoked in 1982 to 2003 directly correlates to a linear reduction in outdoor ambient air ETS concentrations. See Appendix D for explanation of assumptions and the method used to calculate the 2003 Los Angeles outdoor ambient ETS particle concentrations.

Using the estimated annual average ETS fine particle concentration data from the two previous studies (Schauer *et al*., 1996 and Rogge *et al*., 1994), staff estimated the annual average Los Angeles ETS particle concentrations to range from 0.06 to 0.10 ug/m^3. In addition, and to compare with other outdoor ambient nicotine results, we have adjusted the fine PM concentrations by the ratio of fine PM to nicotine (8.1:1) (Nelson, 1994; Martin *et al*., 1997) to calculate a range of Los Angeles annual average nicotine concentrations of 0.008 to 0.013 μg/m^3 (see Table V-4).

Table V-4

Estimates of ETS Outdoor Ambient Concentrations

Method/Reference	Data Year	Concentrations ($\mu g/m^3$)	
		Fine $PM_{2.5}$	nicotine
fine PM – Source Apportionment Schauer *et al*., 1996	1982	0.21 $\mu g/m^3$ annual average	*0.026 $\mu g/m^3$ annual average
Iso- and anteisoalkanes – measurement Rogge *et al*., 1994	1982	0.28 – 0.36 $\mu g/m^3$ annual average	*0.035 – 0.044 $\mu g/m^3$ annual average
Nicotine – measurement Eisner *et al*., 2001	2001	*0.20 $\mu g/m^3$ 7-day median conc.	0.025 $\mu g/m^3$ 7-day median conc.
Nicotine – measurement ARB, 2003	2003	*0.11 – 25 $\mu g/m^3$ 8-hour range *0.073 – 0.97 $\mu g/m^3$ 8-hour background	0.013 – 3.1 $\mu g/m^3$ 8-hour range 0.009 – 0.12 $\mu g/m^3$ 8-hour background
Los Angeles background – Estimate ARB, 2004	2003	0.06 – 0.10 $\mu g/m^3$ annual average	0.008 - 0.013 $\mu g/m^3$ annual average

* Calculated value using: $PM_{2.5}$/Nicotine concentration = 8.1 (see Appendix C)

D. INDOOR AIR CONCENTRATIONS OF ETS

1. Introduction

As discussed earlier in the chapter, ETS is a complex mixture and measurement of all or most of its components is not practicable. Two main approaches have been used to quantify indoor concentrations and exposure: direct methods, using personal monitors and/or measuring biomarkers, and indirect measurement methods, using ETS markers and/or mass balance modeling. Personal monitors measure ETS exposure at an individual's breathing zone. Biomarkers, which are ETS components or their metabolites found in human physiological fluids, are the best direct means of assessing ETS exposure. However, biomarkers are difficult to obtain relative to indirect markers because they require collection of human body fluid samples, such as urine, serum, or saliva. Thus, indirect methods are the predominant means for quantifying indoor concentrations and exposure.

ETS markers should be unique to tobacco smoke, show similar emission rates across cigarette brands, and be found in similar proportions to the ETS component they propose to trace. Nicotine and RSP are the most widely used markers for the presence and concentration of ETS in indoor environments. Nicotine particularly has been favored because it is specific to ETS and because, in its vapor phase, it is fairly simple and inexpensive to measure. However, critics of its use as a marker note that nicotine

in environmental chambers has a different decay pattern than many ETS components: 80-90% is deposited on surfaces within a few hours of emission, whereas RSP is removed largely through building ventilation and thus may vary greatly relative to nicotine over time and with changes in ventilation rates (as reviewed by Daisey, 1999). Sorbed nicotine can be re-emitted from surfaces at significant levels compared to those emitted by active cigarettes, as determined by long-term sampling in areas where smoking occurs regularly (Daisey, 1999). Singer *et al.* (2003) tested the sorption effects of nicotine and other compounds and potential ETS exposures under habitual smoking conditions. The results indicate that indirect exposures (residual ETS when non-smoker is present after smoker finishes) accounted for a larger fraction of exposures for nicotine and other sorbing compounds versus non-sorbing ETS components. Indirect routes accounted for about 50 percent of potential nicotine exposures during the non-smoking periods. Despite the sorption and desorption of nicotine, it is still a very useful marker for ETS.

Respirable suspended particulates are another commonly used marker. As noted in the 1997 Cal/EPA report, different authors may refer to RSP as either $PM_{2.5}$, PM_{10}, or size cuts in-between. ETS-related particles typically are less than one micron in diameter, so are included in both $PM_{2.5}$ and PM_{10}. Unlike nicotine, RSP is not specific to cigarette smoke, as it is also produced by other indoor combustion sources. However, typically these sources contribute much less to indoor RSP levels than does ETS (Cal/EPA, 1997), although some styles of cooking may contribute notably to residential RSP levels (Fortmann *et al*., 2001).

Models based on mass balance are another means of indirectly assessing ETS exposure. Although it has been argued that predictions derived from these models are too situation-specific to be generalized to the overall population (Cal/EPA, 1997), several recent studies have taken steps toward designing models with greater general applicability. For example, recent studies (e.g. Klepeis *et al*., 2001a and Klepeis, 1999) have taken survey data of California human activity patterns and combined them with models based on the mass balance equation to generalize to a larger population. The Klepeis *et al.* (2001a) study also incorporated point estimates of ETS-related $PM_{2.5}$ concentrations in various microenvironments, thereby allowing even greater ability to predict population-wide patterns. Another study (Repace *et al*., 2000) used actual measured volumes and air exchange rates for 316 California homes to generalize indoor ETS measurements to a broader population.

Three comprehensive reviews on ETS concentrations in indoor air were published in the late 1990's. The most recent review of indoor ETS concentrations, the OEHHA 1997 report: *Health Effects of Exposure to Environmental Tobacco Smoke* (later adopted by the National Cancer Institute's 1999 report entitled *Health Effects of Exposure to Environmental Tobacco Smoke: The Report of the California Environmental Protection Agency*), includes studies conducted in California prior to 1996 with findings from two earlier major reviews (discussed below). This OEHHA report is the basis for information presented in this section.

A 1992 U.S. EPA report, *Respiratory Health Effects of Passive Smoking: Lung Cancer and Other Disorders,* examined studies that reported indoor concentrations of various ETS-related air contaminants, focusing primarily on nicotine and RSP. This report reviewed studies published primarily in the 1980's and early 1990's that measured contaminant levels across a broad range of different microenvironments.

An extensive compilation of measured indoor levels of ETS-related components also is presented in a book by Jenkins *et al*. (2000), entitled *The Chemistry of Environmental Tobacco Smoke: Composition and Measurement*. Concentrations of nicotine, RSP, carbon monoxide, nitrogen oxide, formaldehyde, volatile organic compounds, and polycyclic aromatic hydrocarbons are compared between smoking and control areas across a wide variety of indoor environments. The data summarized were published mainly from about 1980-1991, and were collected both in the United States and abroad.

Since these reviews were published, smoking habits in California have changed. Initiation of the California Tobacco Control Program in 1988 and passage of the statewide smoke-free workplace law in 1995 have led to a reduction in smoking by the California population and eliminated smoking at most California indoor workplaces, including restaurants, bars, and gaming clubs. The proportion of California adults who were daily smokers declined from 15.9% in 1990 to 13.0% in 1999 (Gilpin *et al*., 2001). Data also indicate that those who continue to smoke are smoking fewer cigarettes than they had in the past.

Consequently, although the following discussion will reference concentrations before 1996, the emphasis has been placed on indoor ETS studies published from 1996 forward, and on data collected in California to reflect the recent reduction in smoking prevalence. There are a limited number of new studies that reflect the effects of the ban on smoking in California workplaces. In contrast to the reduction in ETS concentrations in the workplace, the levels of ETS constituents in homes are relatively similar to what they were prior to 1996.

2. Indoor Air Concentrations of ETS Based on Nicotine Measurements

a. Studies of indoor nicotine concentrations presented in the 1997 Cal/EPA report

The U.S. EPA review (1992) included studies conducted in a wide variety of indoor environments in the United States. Results of those studies indicate that average indoor concentrations of nicotine prior to 1992 ranged about 100-fold, from 0.3 to 30 $\mu g/m^3$. The average concentrations in residences with one or more smokers typically ranged from 2 to 11 $\mu g/m^3$, with high values of up to approximately 14 $\mu g/m^3$. In data collected from the mid-1970's through 1991, average concentrations of nicotine in the workplace were similar to average concentrations measured in residences, but workplace concentrations ranged to levels about twice as high as those in homes. The concentrations of nicotine were found to increase as a function of the number of smokers present and the number of cigarettes consumed (U.S. EPA, 1992: Section 3.3.1.2 and pages 3-32 to 3-33).

A study by Marbury *et al*. (1990) measured the smoking activities of parents and nicotine concentrations in the activity rooms and bedrooms of 48 children under age two. The results show that activity and bedroom concentrations of nicotine in the children's homes increased with the number of cigarettes smoked in the home by parents. Weekly average concentrations ranged from 0.15 $\mu g/m^3$ in an activity room of a non-smoker to 12.11 $\mu g/m^3$ in the activity room of both parents smoking.

In the Guerin *et al* (1992) comprehensive survey of indoor measurements, the maximum nicotine concentrations were 30 $\mu g/m^3$ or less in over 50 percent of the studies examined, and less than 100 $\mu g/m^3$ in 90 percent of the studies. Average indoor nicotine concentrations when smoking was present ranged from approximately 1 $\mu g/m^3$ to 40 $\mu g/m^3$, with maximum concentrations substantially greater.

One study reviewed in Guerin *et al*. (1992) clearly illustrates the change in nicotine concentrations when a workplace smoking ban is implemented. Vaughan and Hammond (1990) measured nicotine levels in an office building before and after implementation of smoking restrictions. Prior to the restriction, average nicotine measurements at non-smoker desks were 2.0 $\mu g/m^3$. Seven weeks after smoking was restricted, average nicotine measurements at non-smoker desks were 0.1 to 0.3 $\mu g/m^3$. Off-gassing from smokers' clothing and office furniture may have contributed to residual airborne nicotine levels. There was also evidence of spillover from a smoking floor to a non-smoking floor through a shared air handler. Smoking was allowed at the snack bar, which led to an increase in nicotine levels in that area from about 11 $\mu g/m^3$ before restrictions to an average of 85.4 $\mu g/m^3$ after restrictions. On one occasion, 179 $\mu g/m^3$ was measured in the snack bar area. The non-smoker desks on this floor had the highest non-smoker nicotine readings for the study, with a maximum of 0.7 $\mu g/m^3$.

In the Cal/EPA 1997 report, the new studies discussed in the review reported personal nicotine concentrations rather than indoor air concentrations. Individuals who were reported as exposed to ETS had personal air exposures ranging from 0.69 to 3.27 $\mu g/m^3$. Individuals who did not report exposure to ETS were still exposed to average nicotine concentrations of 0.05 and 0.22 $\mu g/m^3$.

In the Particle Total Exposure Assessment Methodology (PTEAM) study, conducted in the early 1990's, sponsored by the U.S. EPA and the ARB, investigators collected exposure data from 178 non-smokers in Riverside, California using indoor and personal monitors with pumps for PM10. They collected vapor-phase nicotine on a filter treated with citric acid. Additional data analyses since 1996 indicate that for participants who reported ETS exposure, personal and indoor nicotine measurements were about 1 $\mu g/m^3$ while those with no reported exposure had concentrations below the limit of detection (0.15 µg/filter, approximately 0.5 $\mu g/m^3$). When Özkaynak *et al*. (1996) performed a stepwise regression on indoor nicotine concentrations (considering air exchange rates, house volume, and number of cigarettes smoked), they concluded that nicotine levels increased by approximately 0.2-0.3 $\mu g/m^3$ for each cigarette smoked (R^2=0.35, N=227). A regression on personal levels of nicotine based on minutes of

exposure to cigarette smoke showed that personal exposure increased approximately 0.013 µg/m^3 for each minute of exposure (R^2=0.37, N=334) (Özkaynak *et al*., 1996).

Table V-5 summarizes the nicotine concentrations measured in smoking environments before 1996, as reported in these review documents.

Table V-5

Summary of Indoor Nicotine Concentrations[1] in Smoking Environments Before 1996

Source	Range of Concentrations (µg/m^3)	Mean Concentration (µg/m^3)	Location
U.S. Environmental Protection Agency review (1992)	~0-~14	~2-~11	Residences
	~0-35	~1-~12	Offices
	~0-70	~6-~18	Restaurants
	~0-83	<1-47	Transportation
	~0-25	<1-~13	Other indoor locations
Guerin *et al*. Review (1992)	0-292	1.6-21	Residences
	0-292	2.0-21	Residences overall[3]
	0.7-69.7	3.8-36.6	Offices
	(0.7-199)	(3.8-75)	(Offices, incl. Cigars)
	0-71.5	1.1-36.6	Offices overall[3]
	(0-199)	(1.1-75)	(Offices overall, including cigars)[3]
	<1.6-43.7	14-15	Restaurants
	0-84.5	2.3-34	Restaurants overall[3]
	≤0.03-112.4	7.1-41	Transportation
	≤0.03-112.4	0.4-1,010[2]	Transportation overall[3]
	0.9-167	11.7-37	Other indoor
	0-167	0.6-106	Other indoor overall[3]
	In over 50% of the studies reviewed, the overall indoor maximum values were ≤30 µg/m^3; in 90% of the studies, maximum values were <100 µg/m^3. [4]		

Table V-5 (cont.)

Source	Range of Concentrations (µg/m^3)	Mean Concentration (µg/m^3)	Location
National Cancer Institute Review (1999)		0.69-3.27[5]	24-hour "breathing zone" for ETS-exposed subjects
		0.96[5]	California residences, 12-hour personal exposures for subjects above level of detection (LOD)
		0.10[5]	California residences without smoking
		1.07[5]	California residences with smoking

1. May include personal exposure data and includes all averaging times.
2. Value falls outside of specified range because ranges and means not reported for all studies.
3. May include nonsmoking values (not specified in review).
4. As cited in the National Cancer Institute review (1999).
5. Values reported in a single study.

b. Studies of Indoor Nicotine Concentrations Since the Cal/EPA 1997 Report

i) Studies conducted in California

In recent studies, investigators have used passive badges to measure personal exposure to nicotine. The passive badges are convenient to use and provide sufficiently sensitive results. In one study, fifty adult asthmatics living in northern California who had reported exposure to ETS were invited to participate in a study to measure their exposure to ETS (Eisner *et al*., 2001). The individuals wore passive nicotine badges for one week. At the end of the week, subjects estimated the time they had spent in different microenvironments containing ETS while they were wearing the passive badge. The subjects' self-reported exposure times were compared to actual measured levels. The median personal nicotine level for the week was determined to be 0.05 µg/m^3 (range: 0-3.69 µg/m^3) for those participants reporting any indoor exposure to ETS. Data analyses based on personal ETS concentrations and time spent in various locations estimate the following nicotine concentrations for each microenvironment: home concentrations, 0.61 µg/m^3; outdoor work concentrations, 0.03 µg/m^3; and other outdoor concentrations, 0.025 µg/m^3 (Eisner *et al*., 2001).

In another study, nicotine concentrations in 50 homes with infants ranged from 0-16.55 µg/m^3, with a median of 0.40 µg/m^3. Investigators mailed a passive nicotine monitor to each home, then instructed participants over the telephone on placing the

monitor in the home. The results indicate that 68 percent of the women in these homes reported that they smoked, while 32% reported that only their partners smoked (Hudmon et al., 1997).

ii) Studies of nicotine conducted outside of California

Siegel and Skeer (2003) reviewed existing indoor data on exposure to ETS in free-standing bars, bowling alleys, billiard halls, betting establishments, and bingo parlours (5 B's) as determined by nicotine air concentration levels and compared them to levels of exposure in offices, homes, and restaurants. Studies were included in the review if they reported a mean concentration of nicotine measured in at least one of the 5 B's. A weighted average of the mean nicotine concentrations reported in each of the studies was calculated for each of the 5 B's. From this data, it was determined that nicotine concentrations in the 5 B's ranged from 9.8 $\mu g/m^3$ to 76 $\mu g/m^3$ and were 2.4 to 18.5 times higher in than in offices or residences, and 1.5 to 11.7 times higher than in restaurants.

Jenkins *et al.* (1996) used personal monitoring to determine ETS exposure in 16 U.S. cities, including Fresno, CA. Study participants wore one personal monitor at the workplace, and another monitor away from the workplace. Data were collected for eight different ETS markers. Exposures to nicotine ranged from 0.055 $\mu g/ m^3$ when not exposed to smoking at either the workplace or home to a mean of 3.27$\mu g/ m^3$ when exposed both at work and home. However, the study population in Jenkins *et al.* (1996) differed notably from the U.S. population on several accounts. The study population over-represented females by about 25%, and had nearly double the "some college" population and about 50% more college graduates relative to the U.S. population. Concomitant with the differences in education level, the study population also had a higher income level and a higher percentage in management and professional positions relative to the U.S. population, and therefore a lower percentage of participants in service jobs, production, labor, and other blue-collar positions. The population sampled is known to have a lower proportion of smokers than the population at large; thus the somewhat low levels measured are not suprising. The study sample also differed further from the California population: minority populations (African American, Hispanic) were under-represented in the study relative to the U.S. population, and California has a substantially greater percentage of minority residents relative to the U.S.

Graves *et al*. (2000) used data from Jenkins *et al.* (1996) to further examine ETS-associated nicotine levels encountered by non-smokers at reportedly non-smoking workplaces. The authors compared subjects from non-smoking workplaces/non-smoking households versus those from non-smoking workplaces/smoking households. Graves *et al*. (2000), found that personal breathing zone concentrations of nicotine showed median values of 0.06 $\mu g/m^3$ with a mean value of 0.24 $\mu g/m^3$ when ETS exposure was reported in the home (n=235) versus a median of 0.02 $\mu g/m^3$ and mean of 0.08 $\mu g/m^3$ for non-smoking homes (n=813). Thus, nicotine exposures were significantly higher for individuals from self-reported smoking homes as opposed to those who reported no home ETS exposure. The Graves *et al*. results are somewhat low relative to those reported by Jenkins *et al*. in their earlier papers; this was attributed

to deletion of some data points due to misclassification, apparatus failure, and other data clean-up procedures.

Maskarinec and colleagues (2000) examined ETS exposure in restaurant and tavern workers in the vicinity of Knoxville, Tennessee. The authors collected area samples of nicotine in 32 non-bar areas and 53 bar areas and obtained average concentrations of 6.01 $\mu g/m^3$ and 14.4 $\mu g/m^3$, respectively.

Nicotine concentrations have been compared in many smoking and non-smoking environments. Hammond (1999) recently conducted a review of the available literature to assess levels of ETS in a wide variety of workplaces in the United States. The author focused on studies from 1984 to 1999 that used nicotine as an ETS tracer. Comparison among work sites that allowed, restricted, or banned smoking showed that locations with smoking bans had the lowest exposure levels; typically nicotine concentrations were less than 1 $\mu g/m^3$. Conversely, higher levels were found in locations where smoking was allowed; generally 2-6 $\mu g/m^3$ in offices, 3-8 $\mu g/m^3$ in restaurants, and 1-3 $\mu g/m^3$ in blue-collar workplaces. In the homes of smokers, mean nicotine values ranged from 1.50 – 5.80 $\mu g/m^3$ and median values ranged from 1.0 to 3.3 $\mu g/m^3$.

In another study, investigators used passive nicotine badges in a study of homes for a weeklong period to correlate the reported number of cigarettes smoked with measured nicotine levels (Glasgow *et al.,1998)*. This study had 39 participants who lived in homes where smoking occurred; 87 percent were smokers. An average of 148 cigarettes was smoked in each home during the week. The mean measured nicotine value was 5.4 $\mu g/m^3$ and ranged from 0.02 to 29.2 $\mu g/m^3$. Households that reported no indoor smoking during the monitoring period had significantly lower nicotine levels than those that reported smoking (0.10 $\mu g/m^3$ vs. 6.3 $\mu g/m^3$, respectively). For households reporting 50 or fewer cigarettes per week, nicotine concentrations were below 3 $\mu g/m^3$.

Trout *et al.* (1998) investigated the effects of ETS exposure on employees at a casino in Atlantic City, New Jersey. As part of this study, ten general area air samples were tested for nicotine vapor. On a Thursday evening, the area time weighted average for nicotine had a geometric mean of 8 $\mu g/m^3$ and a range of 6-12 $\mu g/m^3$; on a Friday evening, the mean and range were 11 $\mu g/m^3$ and 8-16 $\mu g/m^3$, respectively.

Nicotine concentrations from studies published after 1995 are summarized in Table V-6.

Table V-6

Summary of Indoor Nicotine Concentrations in Smoking Environments After 1995

Reference	Number of samples, Averaging time	Location	Concentration ($\mu g/m^3$)			Comments
			Personal		Indoor Mean	
			Range	Mean		
Siegal and Skeer, 2003	940[1] 91 402 4 6 3 27 3	Offices Residences Restaurants Betting establishments Bowling Alleys Billiard halls Bars Bingo Parlours			4.1 4.3 6.5 9.8 10.5 13.0 31.1 76.0	Weighted mean concentrations were reported from all studies in each of the study locations
Eisner *et al*. 2001	20 people 7 people 12 people 1 week (passive)	Places visited by asthmatic adults, CA	0-3.69 (25^{th}-75^{th} quartile)	0.05 0.03[2] 0.61[2] 0[2]		Subjects reporting indoor exposure (12 with outdoor exposure also) Outdoor Work Subjects reporting home exposure Subjects reporting no exposure
Graves *et al.* 2000	235 people 813 people	16 U.S. cities		0.24 0.06[2] 0.08 0.02[2]		Home exposure reported No home exposure reported
Maskarinec *et al.* 2000	32 area 53 area	Knoxville, TN Non-bar Area Bar Area		6.01 14.4		

Table V-6 (cont.)

Reference	Number of samples, Averaging time	Location	Concentration (µg/m^3)			Comments
			Personal		Indoor Mean	
			Range	Mean		
Jenkins et al. 1996*	122	16 U.S. Cities	9.08 = 95%	3.27		Exposure at work & away from work
	149		4.39 = 95%	1.41		Exposure away from work, no exposure at work
	154		2.10 = 95%	0.686		Exposure at work, no exposure away from work
*all data for non-smokers	555 24-h sample		0.173 = 95%	0.055		No exposure to ETS
Hammond, 1999	1 h or greater	Indoor workplaces			<1[3]	Smoking ban
		Offices			2-6 (34.4)	Smoking permitted (90th percentile)
		Restaurants			3-8	Smoking permitted
		Blue-collar workplaces			1-3	Smoking permitted
	5 homes	Smokers' homes			1.5-5.8 1.0-3.3[2]	
Glasgow *et al*. 1998	39 homes, 1 week (passive)	Homes w/ 1 or 2 Smokers			5.4	Overall mean (mean of 148 cigarettes smoked/ week)
					0.02-29.2	Overall range (mean of 148 cigarettes smoked/ week)
					0.10	Homes with no smoking during monitoring period

Table V-6 (cont.)

Reference	Number of samples, Averaging time	Location	Concentration (µg/m^3)			Comments
			Personal		Indoor Mean	
			Range	Mean		
Glasgow *et al*. 1998 (cont.)					6.3 <3	Homes with smoking during monitoring period Actual concentration smoking homes, ≤50 cigarettes smoked/ week
Trout *et al.* 1998	Approx. 8 h	Casino Atlantic City, NJ	6-12 4-15	8 10	 8-16 11	TWA range Geometric mean. Thursday TWA range Geometric mean. Friday
Hudmon *et al*. 1997	50 homes 2 weeks (passive)	Homes with infants			(0-16.55) 0.40[2]	Smoking homes
Ozkaynak *et al*. 1996	334 people 227 homes	Riverside, CA		0.013 ~1 ND[4]	0.2-0.3 ~1 ND	Increase per cigarette smoked Exposure reported No exposure reported

Table V-6 (cont.)

Reference	Number of samples, Averaging time	Location	Concentration (µg/m^3)			Comments
			Personal		Indoor Mean	
			Range	Mean		
Jenkins *et al*. review 2000					0.7-6.1 (0.2-16.7)	Offices, smoking permitted, range of means (range min. & max.)
			(0.21-95th percentile)	0.86		Workers with smoking bans
			(2.21-95th percentile)	0.30		Workers with designated smoking areas
			(15.0-95th percentile)	3.4		Workers with unrestricted smoking
					5.8 (36-95th percentile)	Restaurants
					14.4 (49.6-95th percentile)	Bars/Bar areas
			(28.9-95th percentile)	5.9		Restaurant servers
			(43.6-95th percentile)	14.1		Bartenders

1. Number of establishments sampled
2. Median value.
3. Measured concentrations for most studies.
4. Non-detected

3. Indoor Air Concentrations Based on ETS-Associated Respirable Particulate Matter

a. Studies of Indoor RSP Concentrations Presented in the 1997 Cal/EPA Report

Measurements of ETS-associated RSP from studies prior to 1992 were summarized in the U.S. EPA document (1992: Figures 3-5, 3-8, and 3-10). An extensive compilation of RSP measurements is also given in Guerin *et al*. (1992). The Office of Environmental Health Hazard Assessment document: *Health Effects of Exposure to Environmental Tobacco Smoke*, summarized additional studies that were relevant to California and published by 1995. As with nicotine, these studies may not be representative of current ETS-associated RSP concentrations due to the decrease of smoking in California, particularly at the workplace.

According to the EPA summary, measured concentrations of ETS-associated RSP ranged about 100-fold, from 5 to 500 $\mu g/m^3$ over a wide variety of indoor environments. In residences with one or more smokers, average daily or weekly concentrations of ETS-associated RSP were increased about 20 to 100 $\mu g/m^3$ over concentrations in similar non-smoking environments. Somewhat lower levels are reported in the workplace (offices), with average concentrations ranging from approximately 2 to 60 $\mu g/m^3$ over concentrations in similar non-smoking environments. Both the maximum reported concentrations (1,370 $\mu g/m^3$) measured in any environment and the highest range of average concentrations (approximately 35 to 986 $\mu g/m^3$) were measured in restaurants (U.S. EPA, 1992: Figure 3-8).

Various measurement methods make it difficult to compare RSP results from different studies. Guerin *et al*. (1992) concluded that most RSP levels are less than 100 $\mu g/m^3$ in control or non-smoking environments. However, he noted exceptions to this statement. When smokers are present, RSP levels range from a small increase over background to as much as three times background, or more. Guerin *et al.* (1992) describes RSP in the 100 – 300 $\mu g/m^3$ range as a high concentration, and concentrations above 300 $\mu g/m^3$ as extreme.

Studies highlighted in the Cal/EPA review (1997) reported RSP concentrations consistent with other reviews. Ott *et al.* (1996) measured average RSP concentrations of 56.8 $\mu g/m^3$ above the outdoor concentration in a California sports tavern with smokers present. Jenkins *et al* (1996) reported average 24-hour personal exposures of RSP at 28.7 to 47 $\mu g/m^3$ when smokers were present, and 18.1 $\mu g/m^3$ for individuals who were not exposed to ETS. The NCI (1999) review also reported RSP data from the PTEAM study conducted in Riverside, California (Pellizzari *et al* , 1992). In that study, 12-hour daytime residential PM_{10} concentrations were consistently higher in homes with smokers, than homes without smokers. The average PM_{10} residential concentrations was 125.6 $\mu g/m^3$ when smokers were present, and 87.8 $\mu g/m^3$ without smokers.

Concentrations of RSP reported in studies published before 1996 are summarized in Table V-7.

Table V-7

Summary of Indoor Particulate Matter Concentrations[1] in Smoking Environments Before 1996

Source	Concentrations ($\mu g/m^3$)				Location
	Smoking		Background/Controls		
	Range	Mean	Range	Mean	
U.S. Environmental Protection Agency review (1992)	~5 – 560	~15 - ~95			Residences
	~2.5 - 90	~2.5 - ~60			Offices
	~12 – 1,370	~35 – 986			Restaurants
	~0 – 850	~0 - ~100			Transportation
	~0 – 1,140	~0 – 295			Other indoor
Guerin *et al*. Review (1992)	0.7-3,150	36-700	0-2,050	0.7-300	Residences
	0-1,088	27-720	4-208	6-300	Offices
	0-685[2]	26-690[2]	15-57[3]	24-400	Restaurants
	0-4,980	18-1,000	3-1,830	15-500	Transportation
	<5-6,220	29-1,947	0-2,200	9.1-520	Other indoor
National Cancer Institute review (1999)		56.8			Sports tavern w/smokers
		28.7-47		18.1	24-hr personal exposure w/smokers, background w/out smokers
		125.6		87.8	12-hr home, w/smokers, background w/out smokers

1. Covers a range of averaging times and methods. Studies conducted outside of the United States were excluded from this table when this information could be deduced from the review articles.
2. Mean exceeds maximum value of the range because means and ranges were not reported for all studies.
3. Values from a single study.

b. Studies of Indoor RSP Concentrations Since Cal/EPA 1997 Report

i*) Studies conducted in California*

Several studies examining indoor RSP from smoking in California have been completed since 1995. Most recently, Ott *et al.* (2003) validated a multi-compartment model with real-time measurements of CO, RSP, particle-bound polycyclic aromatic hydrocarbons (PAH), and $PM_{3.5}$ emitted by cigarettes and cigars in a one-bedroom home in Redwood City, CA. When an individual smoked one cigarette in the bedroom, $PM_{3.5}$ levels rose to about 300 $\mu g/m^3$ in 20 minutes, followed by a gradual two-hour decay to background levels. The smoking of three Kentucky reference cigarettes No. 2R1, one after the other, in the bedroom of a home in Menlo Park, CA caused extremely high RSP concentrations with a peak at 5,500 $\mu g/m^3$. RSP measurements were taken simultaneously in the adjacent living room (with the door between the rooms remaining open). Despite the fact that the cigarettes were being smoked in the bedroom, RSP concentrations equilibrated at approximately 2,000 $\mu g/m^3$ between the living room and bedroom after 45 minutes and showed similar decay rates over the next four hours.

Switzer *et al.* (2001) measured ETS pollutants at one-minute intervals in a variety of Northern California public locations, some before and some after smoking was banned. Measurements at a church-sponsored bingo game where smoking was permitted indicated RSP levels were 87 to 348 $\mu g/m^3$ above outdoor levels. When the church banned smoking at its bingo games, measured RSP levels in the same building (on 11 subsequent visits) were at most 15 $\mu g/m^3$ above ambient levels. In general, statistical analysis of the pollutant data, in combination with active cigarette counts, showed that RSP levels increase about 32 $\mu g/m^3$ for each additional active cigarette. Based on 1992-1994 activity data, and using statistical modeling techniques, the investigators estimated that 1.5 % to 3.5% of Californians would receive a 24-hour ETS-particle exposure exceeding 20 $\mu g/m^3$.

Klepeis (1999) measured RSP and carbon monoxide (CO) in a San Francisco restaurant/ bar. Over a two-hour period there was, on average, one smoker actively smoking at a time. This resulted in an average RSP concentration of 68 $\mu g/m^3$ (range: 36–116 $\mu g/m^3$) above background levels (measured just outside of the bar) for an approximately 800 m^3 room.

In another study conducted in San Francisco, California, Klepeis *et al*. (1999) examined the contributions of cigar and cigarette smoke to $PM_{3.5}$ levels in a residence. When a single cigar was smoked in the parlor, a mean $PM_{3.5}$ concentration of 160 $\mu g/m^3$ and a peak of 350 $\mu g/m^3$ were recorded. In contrast, one cigarette smoked in the same room produced mean and peak values of 65 $\mu g/m^3$ and 160 $\mu g/m^3$, respectively. $PM_{3.5}$ emission rates also were calculated in this study: the emission rate for a cigar smoked for 90 minutes was 0.98 mg/min, whereas the cigarette's emission rate was 1.9 mg/min. However, due to the much larger mass and resulting longer duration of the cigar, the total RSP emissions of the cigar were about five times higher than for the cigarette (88 vs. 17 mg)(Klepeis *et al*., 1999).

Ott *et al*. (1996) examined RSP concentrations at a bar (busy sports tavern) in Menlo Park, California. He was fortunate to collect measurements before and after a smoking prohibition took place. Researchers measured PM3.5 inside and just outside of the tavern using a piezobalance; average readings were taken approximately every 2 minutes. During the pre-ban visits, smoking activity was quantified approximately every 7 minutes, and it was determined that an average of 1.17 cigarettes were active at any given time. Results from this study indicated that the average indoor RSP concentration was 56.8 $\mu g/m^3$ above outdoor levels before the ban, 5.9 $\mu g/m^3$ above outdoor levels (a 90% decrease) in the first two months following the ban, and 12.9 $\mu g/m^3$ above outdoor levels (77% decrease compared to the smoking period) in subsequent months. Moreover, RSP concentrations when smoking was allowed were more than 100 $\mu g/m^3$ above outdoor levels on 30.7% of the visits and, less than 20 $\mu g/m^3$ on 23% of the visits. Levels never exceeded 100 $\mu g/m^3$ following the smoking ban. RSP levels were less than 20 $\mu g/m^3$ above outdoor concentrations on 92% of these nonsmoking visits.

The Ott *et al*. report (1996) also determined, through the use of piezobalances, RSP concentrations produced by four cigars smoked in the center of the tavern. No customers were present during this experiment, but ventilation sources (cooking grill ventilation, windows, and doors) were adjusted to the positions typical of business hours. RSP concentrations reached a maximum of nearly 800 $\mu g/m^3$ before the cigars were extinguished; these concentrations decayed to initial levels after approximately 20 minutes.

Klepeis *et al*. (2001b) used the total human exposure model to estimate childrens' exposure to particulate ETS ($PM_{2.5}$). Measured data taken from six locations were used along with activity pattern data from Wiley et al. (1991a) to estimate ETS $PM_{2.5}$ concentrations. Of the data modeled, 66% of children in all locations were estimated to have no exposures to ETS; 21% of children were estiamted to be exposed to concentrations of 0 to 10 $\mu g/m^3$; 8% from 10 to 65 $\mu g/m^3$; and 5% greater than 65 $\mu g/m^3$ (The National Ambient Air Quality Standards, for a 24-hour average for $PM_{2.5}$). The results indicate that although most children are at zero exposures, a significant percentage of children are exposed to ETS concentrations which compare to elevated levels found indoors with smokers present.

ii) *Studies of RSP Studies Conducted Outside of California*

Investigators outside of California are also measuring the effect a smoking ban has on RSP levels. To compare indoor air quality effects of a smoking ban in Delaware, Repace (2004) sampled eight hospitality venues (a casino, a pool hall, and six bars) for respirable suspended particulates ($PM_{3.5}$) before and two months after the ban. Prior to the ban, the average RSP level was 230 $\mu g/m^3$ (about twenty times the average outdoor background level of 11 $\mu g/m^3$). The average RSP measurement at each venue ranged from 34 $\mu g/m^3$ to 686 $\mu g/m^3$. ETS contributed 90-95% of these indoor RSP levels. For comparison, the U.S. Annual National Ambient Air Quality Standard (NAAQS) for $PM_{2.5}$ is 15 $\mu g/m^3$, and $PM_{3.5}$ (which was examined in this study) is closely related to $PM_{2.5}$.

On average, 5% of the patrons at these establishments were actively smoking at any given time. Following the ban, the average RSP concentration reduced to only 9.4% of the pre-ban value (range of averages for each venue: 2.5-119 $\mu g/m^3$), which, with the exception of one venue, was very similar to outdoor levels. Measurements from each venue were collected for approximately 30 minutes using a pump-driven real-time aerosol monitor.

Jenkins *et al*. (1996) measured RSP ($PM_{3.5}$) in the "16 Cities Study previously discussed in the nicotine section of this chapter." Investigators measured personal concentrations for a 24-hr period while subjects were at work and away from work. Due to the method of sample collection, specific concentrations cannot be determined for a specific microenvironment. The mean personal concentration for those in a smoking work environment and a smoking environment away from work was 47.0 $\mu g/m^3$. The mean concentration for those not exposed to smokers was 18.1 $\mu g/m^3$.

Using previously published personal monitoring data collected from 16 U.S. cities, Graves *et al*. (2000) examined ETS-associated ultraviolet-absorbing particulate matter (UVPM) levels encountered by non-smokers at "nonsmoking" workplaces (*i.e*., smoking typically did not occur within 100 feet of the subjects' personal workspaces.) The authors compared subjects from nonsmoking workplaces/nonsmoking households with those from nonsmoking workplaces/smoking households. UVPM median values were 1.07 $\mu g/m^3$ for subjects from smoking homes (n=235) and 0.82 $\mu g/m^3$ for those from nonsmoking homes (n=813) (mean values were 3.27 $\mu g/m^3$ vs. 1.54 $\mu g/m^3$, respectively). These UVPM exposures were significantly higher for individuals from self-reported smoking homes as opposed to those who reported no home ETS exposure**.** As discussed earlier, these results are lower than other studies that measured PM-related ETS exposures.

In an ETS study conducted in a casino in Atlantic City, New Jersey, Trout *et al.* (1998) measured respirable dust concentrations ranging from undetectable (below the detection limit of 20-30 $\mu g/m^3$) to 90 μ/m^3.

In a study of Knoxville, Tennessee restaurant and tavern employees, Maskarinec *et al*. (2000) measured mean RSP levels of 73 $\mu g/m^3$ in non-bar areas and 135 $\mu g/m^3$ in bar areas. These researchers also determined UVPM concentrations in the two aforementioned settings, recording mean levels of 29.4 $\mu g/m^3$ in non-bar areas and 95.0 $\mu g/m^3$ in bar areas.

Table V-8 summarizes indoor particulate matter concentrations in smoking environments reported in studies published after 1995.

Table V-8

Summary of Indoor Particulate Matter Concentrations in Smoking Environments After 1995

Reference	Number of samples, Averaging time	Location	Measured	Concentration (µg/m^3)		Comments
				Smoking	Non-smoking	
Ott *et al*. (2003)		Home, Redwood City, CA Home, Menlo Park, CA	PM3.5	300 5,500		Bedroom maximum from 1 cigarette Bedroom maximum from 3 cigarettes
Repace (2003)	30 minute real-time	Hospitality venues, DE	PM3.5	230 34-686	 2.5-119	Mean before smoking ban Range of means across venues, before and after smoking ban
Offermann *et al*. (2002)		Minivan, CA	PM5.0	92 1,195		Mean from 1 low-tar cigarette, windows open; outdoor RSP 7 µg/m^3 Mean from 1 low-tar cigarette, windows closed; outdoor RSP 4 µg/m^3

Table V-8 (cont.)

Reference	Number of samples, Averaging time	Location	Measured	Concentration (µg/m^3)		Comments
				Smoking	Non-smoking	
Switzer *et al*. (2001)	1 min sampling intervals	Church bingo games, northern CA	PM3.5	87-348		Increase over outdoor levels before smoking ban (12 visits, 10 min-2 h)
					≤15	Increase over outdoor levels after smoking ban (11 visits)
Jenkins *et al*. 1996*	122	16 U.S. Cities	PM3.5	47.0		Mean personal conc., exposed at work & away from work
	149			33.0		Mean personal conc., exposed away from work only
	154			28.7		Mean personal conc., exposed at work only
*all data for non-smokers	555				18.1	Mean personal conc., no exposure to ETS
Graves *et al*. (2000)	235 people	16 U.S. cities	UVPM	3.27	1.54	Mean, home exposure reported
	813 people			1.07	0.82	Median, no home exposure reported
Maskarinec *et al.* (2000)	32 area	Non-bar area	RSP	73		
			UVPM	29.4		
	53 area	Bar area	RSP	135		
	4+ hours		UVPM	95.0		

Table V-8 (cont.)

Reference	Number of samples, Averaging time	Location	Measured	Concentration (µg/m^3)		Comments
				Smoking	Non-smoking	
Ott *et al*. (1996)	~2 min intervals	Sports tavern, Menlo Park, CA	PM3.5	56.8[1]	5.9	Mean increase over outdoor levels before smoking ban
					12.9	Mean increase over outdoor levels, first two months after smoking ban
					-7.5-71.8	Mean increase over outdoor levels, more than two months after smoking ban
				0-148.8	<20	Range of mean increases over outdoor levels, before and after smoking ban
				>100		30.7% pre-ban visits
				<20		23% of pre-ban visits
				<20		92% post-ban visits
				~800		Maximum from 4 cigars (using piezobalances)

Table V-8 (cont.)

Reference	Number of samples, Averaging time	Location	Measured	Concentration (µg/m^3)		Comments
				Smoking	Non-smoking	
Klepeis (1999)	2 hr duration	Smoking restaurant/ bar, San Francisco, CA		68 36-116		Mean increase over background levels (just outside bar); 1 active smoker on average Range of increases over background levels
Klepeis *et al*. (1999)		Home, San Francisco, CA	PM3.5	160 350 65 160		Mean concentration in parlor, 1 cigar smoked Maximum concentration in parlor, 1 cigar smoked Mean concentration in parlor, 1 cigarette smoked Maximum concentration in parlor, 1 cigarette smoked
Trout *et al.* 1998		Casino, Atlantic City, NJ	RSP	<20 – 90	--	Range

Table V-8 (cont.)

Reference	Number of samples, Averaging time	Location	Measured	Concentration (µg/m^3)		Comments
				Smoking	Non-smoking	
Jenkins *et al*. review 2000			RSP	27-99		Offices, smoking means
			RSP		22.8-30	Offices, non-smoking means
			RSP		38	Restaurants, non-smoking mean
			RSP	57-190		Restaurants, smoking means
			TSP	502		Nightclubs, mean
			RSP		19.7-28	Workers, non-smoking home means
			RSP	44.1-89		Workers, smoking home means
			RSP		30	Workers, non-smoking workplaces mean
			RSP	30-67		Workers, smoking workplaces, means
			RSP	109		Waiters, pers. exposure mean
			RSP	151		Bartenders, pers. exposure mean

1. 1.17 active cigarettes, on average.

4. Indoor Air Concentrations Based on Measurement of Other ETS Constituents

a. Studies of Other ETS Constituents Presented in the 1997 Cal/EPA Report

Environmental tobacco smoke contains numerous hazardous air pollutants (HAPs) and toxic air contaminants (TACs). Concentration data for select constituents of public health concern, including *N*-nitrosamines, benzene, benzo[a]pyrene and total polycyclic aromatic hydrocarbons (PAHs), carbon monoxide, formaldehyde, and toluene are presented in U.S. EPA (1992: Table 3-3 and Figure 3-3), as are references to the literature (U.S. EPA, 1992: Section 3.3.1). An extensive compilation of data from measurements of a variety of ETS-derived constituents is also given in Guerin *et al*. (1992).

b. Studies of Other ETS Constituents Since Cal/EPA 1997 Report

i) Studies Conducted in California

Several studies have been published since 1995 that report concentrations of other ETS constituents in ETS environments, including several conducted in California. Particle-bound PAHs were measured in a multiple pollutant study conducted in California by Ott *et al*. (2003). When one cigarette was smoked in the bedroom of a small home in Redwood City, concentrations of PAHs peaked in the bedroom at approximately 0.07 $\mu g/m^3$ (door was closed) after 20 minutes before slowly decaying over a 2-hour time period. When three cigarettes were smoked, one after the other, in another home in Menlo Park, the PAH level peaked at about 1 $\mu g/m^3$ in the bedroom, this time with the door open to the rest of the house.

Carbon monoxide (CO) is another constituent of tobacco smoke. In contrast to the large database available on pollutant concentrations from cigarette smoking, much less is known about the levels of pollutants due to cigar smoke. Consequently, Klepeis *et al*. (1999) measured concentrations at a cigar social in a well-ventilated private club in suburban San Francisco attended by about 50 people. The average CO concentration was about 6 ppm (range: 5-11 ppm), with the highest concentration measured on a balcony, in the main hall where 18 individuals were smoking. Corrected for ambient CO levels, the authors estimated that the active smokers contributed 4.5 ppm of CO, which was about the same concentration that was measured in freeway rush-hour traffic en route to the event. At a second event, held at a restaurant in downtown San Francisco and attended by 40 people, CO levels were 13 to 17 ppm with about 24 active smokers. The CO concentration was 10 ppm (9 ppm over ambient levels) averaged over the entire 3.3 hr visit, during which over 100 cigars were smoked. If the social event had lasted for 8 hours, it could have exceeded the U.S. EPA's NAAQS of 9 ppm over an 8-hour period.

Additionally, Klepeis *et al*. (1999) investigated the contributions of cigar smoke to indoor levels of CO and particle-bound ($PM_{2.5}$) PAHs in various locations around San Francisco, California. Cigars were machine-smoked in an office for an average of 19 minutes each (range: 7-40 min), resulting in peak CO concentrations ranging from 3 to 19 ppm. One hour time-averaged concentrations exceeded 8 ppm for six out of seven cigars when the air exchange rate was below 2 air changes per hour (ach). Average CO emissions for the cigars ranged from 14 to 140 mg/min, with total emissions ranging from 630-1200 mg/cigar. These values are substantially higher than the total CO emissions of 40-70 mg typically reported for cigarettes (Klepeis *et al.*, 1999).

Emission rates for PAHs were compared in a study conducted in a residence. The PAH emission rate for a cigar smoked for 90 minutes was 0.0042 mg/min, whereas the cigarette's emission rates was 0.015 mg/min. However, total PAH emissions from the cigar were about three times higher than that of the cigarette (0.38 vs. 0.14 mg, respectively) due to the much larger mass and smoking duration of the cigar (Klepeis *et al*., 1999).

In another study examining cigar emissions, Ott *et al*. (1996) measured carbon monoxide (CO) concentrations resulting from cigar smoke in a sports tavern in Menlo Park, California using Langan L16 monitors. Four cigars were smoked in the center of the tavern when no customers were present but with all ventilation sources (cooking grill ventilation, windows, and doors) adjusted to simulate "typical" conditions during business hours. CO levels, measured at three different locations in the tavern, reached peak levels of approximately 4.5 to 6.0 ppm after about 10 to 15 minutes.

While emissions from cigars and cigarettes vary in magnitude, the variability in emissions between brands of cigarettes is relatively low. Daisey *et al*. (1998) conducted a chamber study testing six of the most popular commercial brands in California and one reference cigarette for emissions of 21 different air toxics and other airborne compounds, including volatile organic compounds (VOCs), nicotine, aldehydes, and airborne particulate matter (estimated to be $PM_{2.5}$). Diluted sidestream smoke (produced by a smoking machine that smoked three cigarettes sequentially) was used to approximate ETS aging in a room-sized chamber, and a mass-balance model was used to generate estimates of indoor concentrations. Among the VOCs, acetaldehyde and formaldehyde displayed the highest emission factors (average emission factors 3,340 ng/mg tobacco and 2,040 ng/mg tobacco, respectively), and PM showed an emission factor of 12,400 ng/mg. These results suggest that ETS has a substantial influence on indoor concentrations of these compounds.

ii) Studies of Other ETS Constituents Conducted Outside of California

Two noteworthy studies measuring PAH concentrations were recently conducted in the eastern United States. Repace (2003) measured particulate polycyclic aromatic hydrocarbons (PPAH) at eight hospitality venues in Delaware before and two months after a smoking ban took effect. Prior to the ban, the average PPAH concentration was 134 ng/m^3 (averages for each venue ranged from 44 to 249 ng/m^3), about five times the

outdoor background level of 27 ng/m^3. ETS was responsible for 85-95% of these PPAH levels. Following the ban, the average PPAH level was 4.7% of the pre-ban value (range of average values: 1.3-11 ng/m^3), which was basically indistinguishable from outdoor levels. Measurements were collected for approximately 30 minutes using a pump-driven real-time particle-bound polycyclic aromatic hydrocarbon monitor.

In a paper published in 1999 by Jane Chuang *et al*.,children's exposures to PAHs were investigated in low-income rural and inner-city areas in North Carolina. The researchers determined that potentially carcinogenic PAH concentrations were significantly higher in smokers' homes than in nonsmoking homes (geometric mean: 6.14 ng/m^3 vs. 1.38 ng/m^3, respectively)

In the 16 Cities Study (Jenkins *et al.*, 1996) previously discussed, a number of ETS constituents were measured as indicators of ETS. In addition to nicotine and RSP, these included 3-ethenyl pyridine, myosmine, ultraviolet absorbing PM (UVPM), fluorescing PM, scopoletin, and solanesol. These indicators generally tracked expected ETS exposure levels, measuring highest in personal exposures of those who worked and lived in smoking environments and lowest in personal exposures of those living and working in non-smoking environments.

5. ETS Concentrations in Vehicles

Vehicles provide small enclosed environments that can result in extremely high exposure to ETS when smokers are present. Investigators have used both direct and indirect methods to determine ETS levels in vehicles. Offermann *et al.* (2002) measured levels of particulate matter (less than 3 µm in diameter) resulting from an individual smoking a single low-tar cigarette inside a minivan under different ventilation conditions. Observed air exchange rates ranged from 4.0 ach for windows closed and ventilation off to 71 ach for windows open and ventilation off. During smoking, average ETS-RSP levels were 92 µg/m^3 when the windows were open and 1,195 µg/m^3 when the windows were closed. The outdoor respirable particulate matter concentration during these tests ranged from 4 to 7 µg/m^3. The increase in inside vehicle concentrations over that found outdoors was 13 times greater with the driver's window open/ventilation off, 115 times greater with windows closed/ventilation on, and 300 times greater with windows closed/ventilation off.

Modeling analyses also indicate that particulate matter from ETS can be extremely high in vehicles. Based on field data taken from the literature, Klepeis *et al*. (2001) used a modeling approach to calculate a mean ETS-particle ($PM_{2.5}$) point estimate of 2,000 µg/m^3 in vehicles.

Park *et al.* (1998) used a modeling approach based on cigarette emissions and ventilation rates to estimate RSP and formaldehyde levels in vehicles. Levels of ETS constituents in an automobile were estimated under simulated "stop and go" driving conditions. Three different automobiles were tested under a variety of ventilation conditions to calculate air exchange rates. Using ETS emission values obtained from a

1986 National Research Council (NRC) report, the authors calculated that RSP and formaldehyde levels could reach peak levels of 2.06 mg/m^3 and 0.13 mg/m^3 (0.11 ppm), respectively, if a person smoked in an automobile (with one window 50% open) for 6 minutes while driving at 20 mph and 2 min while stationary. The formaldehyde concentration would exceed the NIOSH recommended maximum occupational level of 0.1 ppm. Furthermore, the simulations predicted that with the windows closed and with smoking occurring for 6 minutes of driving at 20 mph and 4 minutes of stopping, RSP could peak at 4.36 mg/m^3 and formaldehyde could reach 0.41 mg/m^3 (0.33 ppm). Thus, the researchers concluded that in-vehicle ETS exposures could be quite high when an automobile is stationary.

6. Modeling Studies to Estimate Indoor Air Concentrations of ETS

Models are a useful tool to estimate indoor concentrations of ETS based on source strength (number of cigarettes smoked), air exchange rates, and the volume of a room. The models can be used with population surveys and questionnaire results to determine patterns of cigarette use and exposure to cigarette constituents in different indoor environments. This approach tends to be much less costly and time consuming than direct exposure assessment. One drawback of models is that they have not yet been systematically validated by comparison with actual exposure measurements (Klepeis, 1999). However, the database of exposure-related information (e.g. survey data) that can be incorporated into the models is rapidly expanding, and as a result, models will continue to increase in reliability in predicting exposures under a variety of conditions (Klepeis, 1999).

Nazaroff and Singer (2002) used a material-balance model to estimate exposures of juveniles and non-smoking adults to 15 Hazardous Air Pollutants (HAPs) contained in ETS. The model incorporated published values on smoking behavior, housing, and demographics along with new emission measurements. Taken in combination with health-based guidelines, these results suggest that three aldehydes (acrolein, acetaldehyde and formaldehyde) pose particular long-term risks to non-smokers who live in a household with smokers. The authors estimate that the entire population of non-smokers in the U.S. living with smokers inhales a total of 260 kg of acrolein per year. Inhaled acrolein from all U. S. ambient sources is estimated at about 300 kg/year; thus, indoor ETS alone contributes about as much acrolein to overall human intake as all outdoor sources combined. Similarly, nationwide, the contribution to human inhalation intake of acetaldehyde from ETS in homes is similar to the intake from ambient air. ETS is a strong source for formaldehyde; however, formaldehyde emissions to ambient air from other sources are stronger contributors to human inhalation exposure than ETS in homes.

Activity pattern data can be combined with field measurements to generalize results of small-scale ETS studies to a larger population. Klepeis *et al*. (2001a) conducted such an analysis based on activity data from the National Human Activity Pattern Survey for California (NHAPS-CA) sponsored by the U.S. EPA in the mid-1990's and the ARB California Activity Pattern Survey collected in the late 1980's. They estimated that from the late 1980's to mid 1990's there was about a 20% overall decrease in the percentage

of Californians exposed to smoking across all locations. However, in vehicles, the decrease over time was estimated to be only one percent. Additionally, the reduction in exposure in residences showed a smaller decrease (9%) than the overall reduction across locations. Klepeis *et al.* (2001a) calculated point estimates of ETS-particle ($PM_{2.5}$) concentrations using field measurements from several studies. Estimated mean $PM_{2.5}$ concentrations are as follows: residence, 30 $\mu g/m^3$; office-factory, 0 $\mu g/m^3$; bar-restaurant, 100 $\mu g/m^3$; other indoor, 5 $\mu g/m^3$; in vehicle, 2,000 $\mu g/m^3$; and outdoor, 0 $\mu g/m^3$.

Burke *et al*. (2001) used the Stochastic Human Exposure and Dose Simulation (SHEDS-PM) model to predict $PM_{2.5}$ exposures in Philadelphia, Pennsylvania. This stochastic model randomly samples different input distributions to estimate population exposure to particulate matter. Burke *et al*. Estimated that one third of the population under study was exposed to ETS in homes. Investigators further calculated that, when the effects of a single smoker were added to the distribution of indoor-residential $PM_{2.5}$ exposure, the exposure of those in the 75^{th} percentile would increase by about 10 $\mu g/m^3$ and those in the 90^{th} percentile by about 28 $\mu g/m^3$. Moreover, the median overall $PM_{2.5}$ exposure for those who were not exposed to ETS in their residences was 16 $\mu g/m^3$, compared to 20 $\mu g/m^3$ for the general population; for the 90^{th} percentile, the values were 32 vs. 59 $\mu g/m^3$, respectively.

Modeled RSP concentrations associated with ETS indicate that 70 to 90 percent of homes with one smoker would violate the annual NAAQS for $PM_{2.5}$ of 15 $\mu g/m^3$ based on smoking alone. A model used by Repace *et al.* (2000) predicted annual average residential ETS-RSP levels between 20 and 35 $\mu g/m^3$. Model inputs were based on air exchange rates measured in southern California homes, an estimate of 14 mg RSP emitted per cigarette, and assuming 13 cigarettes were smoked per day in a home. The authors estimate that, for homes with very small volumes and poor ventilation, 10 percent would exceed an annual average of 50 $\mu g/m^3$ and one percent would exceed 85 $\mu g/m^3$ (Repace *et al*., 2000).

Models predict that Californians are exposed to less ETS today than they were in the 1980's. Miller *et al*. (1998) examined exposures of nonsmoking Californians to 17 toxic air contaminants (TACs) known to be present in ETS. These investigators used concentration data for a variety of indoor microenvironments (published between 1980 and 1996) in combination with the ARB's activity pattern survey findings (1991, 1992) to model Californians' ETS exposures for the late 1980's and to make predictions for the late 1990's. Two independent methods were used to simulate indoor concentrations: completely-mixed room models and tracer methods (which utilized published concentrations of ETS-related nicotine and respirable suspended particles). The modeling results for the late 1980's predicted that 52% of nonsmoking adults were exposed to ETS on any given day, and that 58-61% of this exposure occurred in residences and workplaces and up to 15% occurred in vehicles. For the 62% of adolescents (ages 12-17) who received exposure, 62-74% occurred in homes, 8-18% was from transportation, and 4-15% was contributed by retail and other indoor environments (e.g. shopping malls, beauty salons, etc.). For the 33% of children (ages

7-11) exposed to ETS, 70-73% of total exposure was in the home, whereas 9-18% occurred in vehicles and 6-7% occurred in others' homes.

Miller *et al*.'s predictions for the late 1990's showed a considerable drop in exposures: 16-19% of adults, 33-35% of adolescents, and 21-23% of children were expected to receive ETS exposure on any given day. Only residences, transportation, and others' residences were examined for the microenvironmental exposure simulations, due to smoking bans in workplaces and public establishments. The results predicted that one's own home would be the major site of exposure for all age groups: 58-69% for adults, 58-66% for adolescents, and 72-83% for children. In California, on average, ETS contributes 4-30% of indoor household concentrations of benzene, ethylbenzene, styrene, o-xylene, and m,p-xylene (Miller *et al*., 1998).

Models indicate residences that allow smoking also have higher PM levels than smoke-free homes. Özkaynak *et al*. (1996) determined that for residences in which smoking was reported, average PM_{10} levels were 30 $\mu g/m^3$ higher than those without smoking. Samples from 31 homes showed that smoking contributed 30% of indoor $PM_{2.5}$ mass and 24% of indoor PM_{10} mass. Investigators used a mass-balance model to estimate a PM2.5 source strength for cigarettes of 13.8 $\pm$ 3.6 mg/cigarette. Data for these analyses were collected in Riverside, CA during the PTEAM study.

7. Summary of Indoor Data

Restrictions on smoking in California from the late 1980's to mid 1990's in workplaces and in public locations such as restaurants, bars, and gaming clubs have led to a reduction in smoking in indoor environments in California, with commensurate reductions in indoor concentrations of ETS and non-smokers' exposure levels. A number of studies published since 1996 have shown that ETS constituents are present at lower concentrations following smoking bans than they were prior to the bans and that levels can be considerably higher in smoking versus comparable nonsmoking areas. Despite California's smoking bans, high indoor ETS concentrations still can be found in smokers' homes and in private vehicles and in some non-compliant public establishments. This is of particular concern because if children are present, they are most likely to be found in these locations and thus may experience high levels of exposure to ETS.

Nicotine results for studies conducted before 1996 and after 1995 indicate mean concentrations have decreased in workplaces and restaurants, but not necessarily in homes. Comparison of mean nicotine concentrations from studies reported in the U.S. EPA Review (1992) and Guerin *et al*. (1992) with data published after 1995 reveals that indoor means have not changed significantly for homes. Results from the earlier studies indicate that residential mean nicotine concentrations ranged from about 2 to 21 $\mu g/m^3$. The newer studies indicate that when smokers are present, nicotine concentrations range from nearly zero to 29 $\mu g/m^3$. The upper end of this range represents a small portion of homes with excessive smoking and probably limited building ventilation. Estimates of mean residential nicotine concentrations are 0.5, 3.0, and 6.0 $\mu g/m^3$ for low, medium, and high concentrations, respectively, based primarily

on measurements taken by Glasgow *et al*. (1998). The recent body of data indicates that those who choose to smoke in their home have remained consistent in their smoking patterns over the years.

When smoking is permitted at a workplace or public place, nicotine concentrations are not as great as they were before 1996. In studies conducted before 1996 mean nicotine concentrations in offices and restaurants ranged from about 1 to 36 $\mu g/m^3$. In a more recent review, Hammond (1999) reported means of 2 to 8 $\mu g/m^3$ for these locations. It apprears that, as smoking has become less accepted social behavior, individuals are not smoking in indoor public locations that permit smoking as much as they did a few years earlier.

Workplace smoking bans are effective in reducing nicotine concentrations. According to the Hammond (1999) review, nicotine levels were two- to six- times lower in indoor workplaces with smoking bans than in offices that allowed smoking (less than 1 $\mu g/m^3$ vs. 2-6 $\mu g/m^3$, respectively). However, certain workplaces, such as the approximately 20% of free-standing bars that are not yet compliant with California's workplace smoking ban (Weber et al., 2003), would likely have higher elevated levels of ETS, based on measurements made across many studies in such locations (Siegel and Skeer, 2003).

Levels of respirable particulate matter (RSP) are generally comparable in both older and newer studies, but slightly lower in the newer studies (relative to 1996). All measured levels tend to be from about 100 to 400 $\mu g/m^3$ in offices and restaurants that allow smoking. Results from the newer studies clearly indicate that a ban on smoking results in lower RSP concentrations in a given environment. For example, $PM_{3.5}$ measurements made at hospitality venues were 230 $\mu g/m^3$ before a smoking ban and 2.5 – 119 $\mu g/m^3$ after implementing a smoking ban (Repace, 2004). RSP levels at a church bingo site in northern California were 87-348 $\mu g/m^3$ with smoking permitted, and less than 15 $\mu g/m^3$ when smoking was banned (Switzer *et al*. 2001). Similarly $PM_{3.5}$ concentrations at a sports tavern in California were 56.8 $\mu g/m^3$ with smoking, and 5.9-12.9 $\mu g/m^3$ with smoking banned. These recent RSP data from smoking locations are somewhat lower than the pre-1996 data, similar to nicotine levels, possibly because it has become less socially acceptable to smoke in most indoor environments. RSP levels are low (<15 $\mu g/m^3$) in indoor locations where smoking is prohibited.

Recent residential RSP ($PM_{3.5}$) measurement is limited to a single study (Ott *et al*., 2003). A level of 300 $\mu g/m^3$ was measured in the bedroom where one cigarette was smoked; 5,500 $\mu g/m^3$ was the maximum bedroom level when 3 cigarettes were smoked.

Very high ETS environments have been measured in vehicles when a smoker is present. RSP levels of 92 $\mu g/m^3$ (with ventilation) to 1,195 $\mu g/m^3$ (without ventilation) were measured inside a minivan (Offermann *et al*. 2002), and estimated to be 2,060 to 4,360 $\mu g/m^3$ under stop-and-go driving conditions in cars (Park *et al*., 1998).

Table V-9 summarizes current indoor levels of nicotine and RSP. Based on recent literature, these are considered to be the best concentration estimates for each microenvironment for calculating total exposure to ETS.

Table V-9

Summary of Indoor Concentrations of Nicotine and RSP Reported After 1995

Environment	Nicotine Concentrations µg/m^3		RSP Concentrations µg/m^3
	Summary	Estimates used for Section E. Scenarios	Summary
Homes			
Non-smoking (CA)	–	–	
Non-smoking (US)	Mean[1]: 0.10	0 – no smoking 0.5 – low	
Smoking (CA)	Mean: 0.61 Range: 0 -16.55	3.0 – medium 6.0 – high	Mean: 65 Peak values: 1 cigarette: 160 - 300 3 cigarettes: 5,500
Smoking (U.S.)	Mean: 1.5 - 6.3 Range: 0.02 - 29.2		
Offices/public buildings			
With smoking (U.S.)	Mean: 2 - 8		
Smoking prohibited (U.S.)	Range 2 - > 35		
Vehicles			
With ventilation (CA)	NA	NA	Mean: 92 (PM_5)
Without ventilation (CA)	NA	NA	Mean: 1,195 (PM_5)
A. Entertainment Venues			
Casinos, betting establishments (U.S.)	Mean: 8 - 11 Range: 6 -16		< 20 - 205
Bowling Alleys (U.S.)	Mean: 10.5		
Billiard halls (U.S.)	Mean: 13		Mean, one hall: 686
Bars, taverns			
With smoking (CA)	Mean: 14 – 31		Mean[2]: 56.8 - 68 Range[2] 0 - 149
With smoking (U.S.)			Mean[2]: 44 - 337
Smoking prohibited (CA)			Mean[2]: 5.9 - 12.9
Bingo Parlors			
With smoking (CA)	Mean: 76.0		Mean[2]: 87 - 348
With smoking (U.S.)			
Smoking prohibited (CA)			≤15

1. smokers' homes with no smoking during monitoring period
2. mean concentration above outdoor levels

E. EXPOSURE ESTIMATION SCENARIOS

1. Introduction

Current smoking practices and California regulations suggest that California children can roughly be divided into three exposure groups: children who have little or no exposure to ETS, children with smoking parents or guardians who take some measures to limit their child's exposure, and children highly exposed to ETS through smoking parents, guardians, or peer groups. Likewise, adults generally have virtually no exposure, experience regular but limited exposure in a public place, or experience substantial exposure through extensive contact with smokers. However, unlike adults, children are often not able to move away from ETS; when with smoking adults, they may not have any choice in whether they are exposed. Similarly, peer pressure can be a significant factor: even non-smoking teens may feel pressure to "hang out" with their smoking friends or be excluded from peer social groups.

These diverse exposure scenarios make a population-weighted, statewide exposure estimate more complex to calculate and less informative than estimates for illustrative scenarios covering a range of exposures. These scenarios are an indication of exposure for some populations over a 24-hour day. Although these scenarios might be more representative of a specific person's daily exposure to ETS, most populations are exposed to low levels of ETS. Eight exposure scenarios are developed below: four for children, and four for adults. The scenarios simulate the ETS exposure a non-smoker would receive in different situations ranging from a low to a high exposure, plus one "maximal exposure" scenario.

2. Background and Calculations

An individual's exposure to an air pollutant in a given environment is dependent on two factors: the concentration of the pollutant in that environment, and the amount of time the individual spends in that environment. Exposure is calculated as the product of these two factors, and the result is a time-integrated exposure estimate (NAS, 1991; Federal Register, 1992). When the concentration is measured in units of $\mu g/m^3$ and time in hours, then the units for exposure are $\mu g\text{-}h/m^3$. *Total indoor air exposure* is the sum of the environment-specific exposures (time-integrated exposures) associated with time spent indoors. *Total 24-hour exposure,* or *total daily exposure,* is the sum of the different exposures experienced by an individual in the many locations they visit during the 24-hour day, both indoors and outdoors.

Another, less often used method of expressing exposure is to estimate the *time-weighted average exposure concentration*. This is essentially the average of the concentrations experienced by an individual across their 24-hour day, and is expressed in concentration units, i.e., as $\mu g/m^3$.

In the exposure scenarios discussed below, exposure estimates are presented for the time-integrated exposure in the major environments visited by the hypothetical person, their total indoor and outdoor exposures, their total 24-hour exposure, and their time-weighted 24-hour average concentration. Nicotine concentration data recently collected by the ARB in public places (see Section C, above) are used as inputs for outdoor concentrations in the simulated exposures. No measurement data is available to estimate outdoor background levels. In these cases, the exposure is assumed to be zero, reflecting a non-smoking environment. In-home levels of nicotine are drawn from the literature discussed above in Section D. Workplace levels are also based on data discussed in Section D.

3. Scenarios

a. Overview

The following exposure scenarios were used to estimate exposures of specific subgroups of the California population with low to high ETS exposures:

Children

C1– Children's Low Exposure Scenario:
Child 8 years old living in a non-smoking household exposed to nicotine while playing outdoors in an area that is adjacent to a neighboring business's smoking area.

C2 – Children's Medium Exposure Scenario:
Child 8 years old living in a smoking household with an average number of cigarettes smoked indoors, and also exposed to nicotine while playing outdoors in an area that is adjacent to a neighboring business's smoking area.

C3 – Children's High Exposure Scenario:
Child 8 years old living in a smoking household with a somewhat high number of cigarettes smoked indoors, and also exposed to nicotine while in the car and at an amusement park.

C4 – Children's Maximal Exposure Scenario:
Child 8 years old, living in a smoking household with a high number of cigarettes smoked indoors, and experiencing the highest outdoor levels measured in ARB's outdoor monitoring tests.

College Student

S1 – College Student Low Exposure Scenario:
Non-smoking college student living in an apartment with a non-smoking roommate who visits a campus designated smoking area.

S2 – College Student High Exposure Scenario:
Non-smoking college student living in an apartment with two smoking roommates, visits the campus designated smoking areas, and goes to the airport on a given day.

Traveler

T1 – Business Traveler's Exposure Scenario:
The non-smoking business traveler is exposed to nicotine while in line at the Automatic Teller Machine (ATM) at the bank, waiting outside the airport terminal, and dining at an outdoor restaurant located next to an office building smoking area.

T2 – Business Traveler's Medium Exposure Scenario:
The non-smoking business traveler is exposed to the same exposure scenarios as in T1, except that he/she spends the first hour of the business lunch with a client at a free-standing bar that is non-compliant with California's workplace smoking ban.

b. Assumptions and Scenario Results

The specific average nicotine concentrations used in the exposure estimation scenarios are indicated in Table V-10. These are averages calculated from ARB's outdoor monitoring scenarios (see Section C).

Table V-10

Summary of Outdoor Nicotine Concentration Data Used in the Estimation of Scenario-Based Exposure

Outside Location	Nicotine Concentration Mean of 1-hour Averages ($\mu g/m^3$)
Airport Terminal	0.72
College Smoking Area	0.051
Local Government Office Complex	0.097
Public Office Building Complex	0.19
Amusement Park Smoking Area	2.4

Children

The assumptions for scenarios C1 and C2, children's low and medium exposures, are:

1. Indoor time at home (12.75 hours) includes all time spent in the home – sleeping, eating, watching television, etc.

2. Time spent indoors at school is 5 hours per day. This includes all classroom/study time indoors.

3. About 1 hour of the day is spent indoors elsewhere (other than at home and school), such as at an after-school care facility.

4. Outdoor time at home (2 hours) primarily includes playing in the yard before and after school.

5. Outdoor time at school (2 hours) includes morning arrival time (15 minutes), recess (15 minutes), lunch time (30 minutes), physical education class (45 minutes), afternoon pick-up time (15 minutes).

6. Outdoor time at other places (1.25 hours) is assumed to be playing outdoors at an after-school care facility or an activity at some other location adjacent to a neighboring business's smoking area.

7. Nicotine concentration for neighboring business smoking area: the mean measured 1-hour average nicotine concentration from the Public Office Building Complex smoking area is used for the nicotine concentration in the neighboring business smoking area. Nicotine concentrations were measured at a Government Office Complex smoking area as well as at a Public Office Building Complex smoking area. The mean 1-hour nicotine concentration was higher at the Public Office building complex. Because the overall objective of this exercise is to characterize the exposures of certain subgroups of the population who are exposed, and because office buildings are more predominant than government buildings, the Public Office Building Complex measurement was selected for use as a surrogate for levels children might be exposed to when playing near a smoking area immediately adjacent to their play area.

8. Nicotine concentration for smoking outdoors at home: because there is no data for ETS concentrations outdoors at home, the mean measured 1-hour average nicotine concentration in a designated smoking area at a college is used as a surrogate for nicotine concentration outdoors at home. The college area concentration resulted from the smoking of 2-6 cigarettes per hour, and thus is reasonable to use as a surrogate for exposure outdoors at home with a smoker present.

9. Nicotine concentration inside the home: is assumed to be 3.0 $\mu g/m^3$. Glasgow (1998) reported homes with 50 or fewer cigarettes smoked per week had indoor

nicotine levels less than 3.0 µg/m^3. Thus, it is estimated that a home with moderate smoking (about 50 cigarettes per week) would have levels up to 3.0 µg/m^3.

C1– Children's Low Exposure Scenario: child 8 years old living in a non-smoking household exposed to nicotine while playing outdoors in an area that is adjacent to a neighboring business's smoking area.

SCENARIO C1: CHILDREN'S LOW EXPOSURE						
Environment	ETS Present	Time Spent in Environment (hours)	Nicotine Concentration in Environment (µg/m^3)	24-hour Time-integrated Exposure in Environment (µg-hr/m^3)	Percent of Total Exposure (%)	Time-weighted Average Concentration (µg/m^3)
Indoor						
Home	No	12.75	0	0		
School	No	5	0	0		
Other	No	1	0	0		
Total Indoor		**18.75**		**0**	**0**	**0**
Outdoor						
Home	No	2	0	0		
School	No	2	0	0		
Other	Yes	1.25	0.19 (a)	0.24		
Total Outdoor		**5.25**		**0.24**	**100**	**0.045**
Total =		**24**		**0.24**	**100**	**0.010**

(a) = Public Office Building Complex mean 1-hour average

Results of this scenario illustrate that young children in non-smoking households would likely have very low exposures, and virtually all of that exposure would result from outdoor smoking.

C2 – Children's Medium Exposure: child 8 years old living in a smoking household with a medium level of smoking indoors, also exposed to nicotine while playing outdoors in an area that is adjacent to a neighboring business's smoking area.

SCENARIO C2: CHILDREN'S MEDIUM EXPOSURE						
Environment	ETS Present	Time Spent in Environment (hours)	Nicotine Concentration in Environment ($\mu g/m^3$)	24-hour Time-integrated Exposure in Environment ($\mu g\text{-}hr/m^3$)	Percent of Total Exposure (%)	Time-weighted Average Concentration ($\mu g/m^3$)
Indoor						
Home	Yes	12.75	3.0 (a)	38.25		
School	No	5	0	0		
Other	No	1	0	0		
Total Indoor		**18.75**		**38.25**	**99.12**	**2.0**
Outdoor						
Home	Yes	2	0.051 (b)	0.102		
School	No	2	0	0		
Other	Yes	1.25	0.19 (c)	0.24		
Total Outdoor		**5.25**		**0.34**	**0.88**	**0.07**
Total =		**24**		**39** (d)	**100**	**1.6**

a) Mid-value, Glasgow *et al*. (1998), see table 5.
b) The mean 1-hour average concentration in a College Outdoor Smoking Area, used as a surrogate for parents smoking in the yard where the child is playing. The number of cigarettes smoked per hour in the College Smoking Area, 2-6, gives a reasonable surrogate for levels when smoking occurs outdoors at the home.
c) The mean 1-hour average concentration in a Public Office Building Complex Outdoor smoking area is used.
d) Totals may not add to exact total due to rounding.

Results of the children's medium scenario illustrate the high impact of living with a smoking parent. The majority of the child's exposure stems from their time spent indoors at home.

The assumptions for Scenario C3, children's high exposure, are:

1. The value of 6.0 $\mu g/m^3$ is used for the indoor home concentration in this scenario, based on Glasgow et al.'s (1998) results showing an average of 5.4 $\mu g/m^3$ and a maximum of 29.2 $\mu g/m^3$ in homes.

2. The child travels for 2 hours each way to and from an amusement park in a car with smoking parents. Because the car is a small confined space, and both parents may smoke at times, the high indoor home nicotine estimate of 6.0 $\mu g/m^3$ from Glasgow et al. (1998, Table 5) is used as a surrogate for the nicotine concentration inside the car.

3. The child spends the times indoors and outdoors at the amusement park as indicated in Scenario C3 below, with a total of 2 of the outdoor hours spent at smoking areas across the day when the parents took smoking breaks.

C3 – Children's High Exposure Scenario: child lives in a smoking household with a high level of smoking indoors is also exposed to nicotine while in the car and at the amusement park.

SCENARIO C3: CHILDREN'S HIGH EXPOSURE						
Environment	ETS Present	Time Spent in Environment (hours)	Nicotine Concentration in Environment ($\mu g/m^3$)	24-hour Time-integrated Exposure in Environment ($\mu g\text{-}hr/m^3$)	Percent of Total Exposure (%)	Time-weighted Average Concentration ($\mu g/m^3$)
Indoor						
Home	Yes	8	6.0 (a)	48.0		
Transit- in car	Yes	4	6.0 (b)	24.0		
Theme Park	No	2	0	0		
Other	No	2	0	0		
Total Indoor + Car		**16**		**72.0**	**93.72**	**4.5**
Outdoor						
Home	Yes	0.5	0.051 (c)	0.026		
Theme Park – Smoking Area	Yes	2	2.4 (d)	4.80		
Theme Park – Non Smoking Areas	No	5.5	0	0		
Total Outdoor		**8**		**4.826**	**6.28**	**0.60**
Total		**24**		**77** (e)	**100**	**3.2**

a) Glasgow *et al.* (1998, see table 5).
b) No data available for inside a car with smokers. Assume high end of home concentration from Glasgow (1998), because passenger cab of car is very small, and both parents may smoke, resulting in high levels of ETS.
c) The mean 1-hour average concentration in a College Outdoor Smoking Area is used as a surrogate for parents smoking in the yard where the child is playing.
d) The mean 1-hour average concentration measured in Amusement Park Smoking Areas.
e) Totals may not add exactly due to rounding to significant digits.

This scenario illustrates the high exposures that would be experienced by a child living in a heavy smoking household with parents or guardians who also smoke in the car. The child's exposure is further increased when the parents visit the outdoor smoking area at the amusement park for smoking breaks. This scenario illustrates the substantial exposure, 4.8 $\mu g\text{-}hr/m^3$, that can occur outdoors at smoking areas visited by many smokers.

C4- Maximally Exposed Scenario

The assumptions for Scenario C4, children's maximally exposed scenario, are:

1. The child makes a day trip to an amusement park with his smoking parents. The time spent in each microenvironment is identical to that in Scenario C3. A total of 2 of the outdoor hours are spent at smoking areas across the day when the parents take smoking breaks.

2. The indoor concentrations are identical to those in C3. The home and in vehicle concentrations are 6.0 μg/m^3 based on Glasgow *et al.'s* (1998) results showing an average of 5.4 μg/m^3 and a maximum of 29.2 μg/m^3 in homes.

3. Outdoor concentrations have been increased to the highest level measured in the ARB monitoring study at specified outdoor smoking areas.

SCENARIO C4: CHILDREN'S MAXIMALLY EXPOSED SCENARIO

Environment	ETS Present	Time Spent in Environment (hours)	Nicotine Concentration in Environment (μg/m^3)	24-hour Time-integrated Exposure in Environment (μg-hr/m^3)	Percent of Total Exposure (%)	Time-weighted Average Concen-tration (μg/m^3)
Indoor						
Home	Yes	8	6.0 (a)	48		
Transit- in car	Yes	4	6.0 (b)	24		
Theme Park	No	2	0	0		
Other	No	2	0	0		
Total Indoor + Car		**16**		**72.0**	**88.59**	**4.5**
Outdoor						
Home	Yes	0.5	0.150 (c)	0.075		
Theme Park – Smoking Area	Yes	2	4.6 (d)	9.2		
Theme Park – Non Smoking Areas	No	5.5	0	0		
Total Outdoor		**8**		**9.3**	**11.41**	**1.2**
Total		**24**		**81** (e)	**100**	**3.4**

a) Glasgow (1998), see table 5.
b) No data available for inside a car with smokers. Assume high end of home concentration from Glasgow (1998), because passenger cab of car is very small, and both parents may smoke, resulting in high levels of ETS.
c) The highest 1-hour average concentration in a College Outdoor Smoking Area is used as a surrogate for parents smoking in the yard where the child is playing.
d) The highest 1-hour average concentration measured in Amusement Park Smoking Areas.
e) Totals may not add exactly due to rounding to significant figures.

This exposure scenario represents the upper limits for children's outdoor exposure. It illustrates an extremely high exposure that would be experienced by a child living in a heavy smoking household with parents or guardians who also smoke in the car. The child's exposure is further increased when the parents visit the outdoor smoking area at the amusement park for smoking breaks. The outdoor exposure in this scenario is approximately double that of Scenario C3 and has the effect of increasing the outdoor exposure from approximately 6% of the total exposure to 11%. Such exposure would occur when a high number of smokers are using the smoking area, wind is minimal, and the child is in close proximity to the parent.

College Student Scenario Assumptions

Two scenarios with college students were developed.

1. In Scenario 1, the student is a non-smoker, lives in a non-smoking household, and is only exposed to ETS when talking with friends at an outdoor area set aside for smokers.

2. In Scenario 2, the student lives in an apartment with two smoking roommates, talks with friends at an outdoor smoking area on campus, and also makes a trip to the airport, where he/she must wait near an outdoor smoking area for a friend whose plane is late. This individual also spends some time outdoors at home with a smoking roommate.

3. Like the children's scenarios, the College Smoking Area input data are used as surrogates for the outdoors at home levels.

4. Outdoors at the airport and outdoors at the college smoking area are taken directly from ARB's measured averages for those areas (see Section B above).

5. In Scenario 2, indoor home levels are assumed to be 6 $\mu g/m^3$, the high exposure level taken from Glasgow (1998) as discussed elsewhere in this chapter, because of the smaller volume of an apartment and the higher ETS concentrations that would be expected.

S1 – College Student Low Exposure Scenario: non-smoking college student living in an apartment with a non-smoking roommate and visits the campus designated smoking areas.

SCENARIO S1: COLLEGE STUDENT LOW EXPOSURE						
Environment	ETS Present	Time Spent in Environment (hours)	Nicotine Concentration in Environment ($\mu g/m^3$)	24-hour Time-integrated Exposure in Environment ($\mu g\text{-}hr/m^3$)	Percent of Total Exposure (%)	Time-weighted Average Concentration ($\mu g/m^3$)
Indoor						
Home	No	8	0	0		
College	No	8	0	0		
Other	No	2	0	0		
Total Indoor		**18**		**0**	**0**	**0**
Outdoor						
Home	No	1	0	0		
College	Yes	2	0.051 (a)	0.102		
Other	No	3	0	0		
Total Outdoor		**6**		**0.10**	**100**	**0.017**
Total =		**24**		**0.10**	**100**	**0.0043**

(a) = The mean 1-hour average concentration in a College Outdoor Smoking Area.

Results from the College Student Low Exposure Scenario again illustrate that non-smokers living in non-smoking households have generally very low exposures, and that whatever exposure they experience is likely to occur from outdoor smoking.

S2 – College Student High Exposure Scenario: non-smoking college student living in an apartment with a smoking roommate and visits the campus designated smoking areas, and goes to the airport that day.

SCENARIO S2: COLLEGE STUDENT HIGH EXPOSURE						
Environment	ETS Present	Time Spent in Environment (hours)	Nicotine Concentration in Environment ($\mu g/m^3$)	24-hour Time-integrated Exposure in Environment ($\mu g\text{-}hr/m^3$)	Percent of Total Exposure (%)	Time-weighted Average Concentration ($\mu g/m^3$)
Indoor						
Home	Yes	8	6.0 (a)	48		
College	No	7	0	0		
Airport	No	1	0	0		
Other	No	2	0	0		
Total Indoor		**18**		**48**	**98.21**	**2.667**
Outdoor						
Home	Yes	1	0.051 (b)	0.051		
College	Yes	2	0.051 (c)	0.102		
Airport	Yes	1	0.72 (d)	0.72		
Other	No	2	0	0		
Total Outdoor		**6**		**0.87**	**1.79**	**0.146**
Total =		**24**		**49** (e)	**100**	**2.036**

a) Indoor Home: Assume high end data for home from Glasgow (1998).
b) Outdoor Home: Use the same input data as the College Smoking Area.
c) College Smoking Area average 1-hour (2-6 cigarettes per hour).
d) Outdoor Airport: Assumes that the student is meeting someone at the airport terminal at a specific outdoor location that is near a designated smoking area, and the plane arrives an hour or so late.
e) Totals may not add exactly due to rounding to significant digits.

This scenario again illustrates the elevated exposures of those living with smoking household members. It also illustrates that adults can experience exposure in several outdoor locations in a day, depending on their specific activity patterns.

Business Traveler's Scenario Assumptions:

1. Non-smoking business traveler has a one-day trip by airline from northern to southern California, for a several-hour business meeting.

2. He/she visits the ATM for cash before driving to the airport, must wait outside the terminal near smokers before getting into the terminal, and travels to southern California.

3. During the meeting, he/she has a business lunch with a business client, sitting outdoors very near the smoking area of a nearby office building. Upon returning to the airport to fly home, he/she again is outdoors near smokers for a time before getting inside the airport.

T1 – Business traveler's exposure scenario: the non-smoking business traveler is exposed to nicotine while in line at the Automatic Teller Machine (ATM) at the bank, while waiting outside the airport terminal, and dining at an outdoor restaurant located next to an office building smoking area.

SCENARIO T1: BUSINESS TRAVELER EXPOSURE						
Environment	ETS Present	Time Spent in Environment (hours)	Nicotine Concentration in Environment ($\mu g/m^3$)	24-hour Time-integrated Exposure in Environment ($\mu g\text{-}hr/m^3$)	Percent of Total Exposure (%)	Time-weighted Average Concentration ($\mu g/m^3$)
Indoor						
Home	No	9	0	0		
Airport	No	2.3	0	0		
Other-bus. Meeting	No	5	0	0		
Other-inside plane	No	3	0	0		
Total Indoor		**19.3**		**0**	**0**	**0**
Outdoor						
Home	No	0.5	0	0		
ATM-Bank	Yes	0.2	0.097 (a)	0.019		
Airport	Yes	1	0.72 (b)	0.72		
Dining	Yes	2	0.19 (c)	0.38		
Other	No	1	0	0		
Total Outdoor		**4.7**		**1.119**	**100**	**0.24**
Total =		**24**		**1.1** (d)	**100**	**0.047**

a) The mean 1-hour average concentration in a Local Government Office Building Complex Outdoor Smoking Area is used at input, assuming a low number of cigarettes smoked near the ATM.
b) The mean 1-hour average Airport Terminal concentration.
c) The mean 1-hour average Public Office Building Complex Outdoor Smoking Area.
d) Total may not add exactly due to rounding to significant figures.

The results for the business traveler scenario indicate that exposure during the day for a non-smoking traveler would be low and occur completely outdoors. Business travelers travelling with smoking co-workers would likely be exposed to higher levels of ETS.

T2 – Business traveler's exposure scenario: in this scenario, the traveler's day is the same as in scenario T1, except that she/he spends the first hour of the business lunch with the client at a free-standing bar that is non-compliant with California's workplace smoking ban, followed by an hour dining in the outdoor section of a restaurant very near the smoking area of a nearby office building.

SCENARIO T2: BUSINESS TRAVELER EXPOSURE - BAR						
Environment	ETS Present	Time Spent in Environment (hours)	Nicotine Concentration in Environment ($\mu g/m^3$)	24-hour Time-integrated Exposure in Environment ($\mu g\text{-}hr/m^3$)	Percent of Total Exposure (%)	Time-weighted Average Concentration ($\mu g/m^3$)
Indoor						
Home	No	9	0	0		
Airport	No	2.3	0	0		
Other-bus. Meeting	No	5	0	0		
Other-inside plane	No	3	0	0		
Visit non-compliant bar	Yes	1	31.1 (a)	31.1		
Total Indoor		**20.3**		**31.1**	**97.1**	**1.53**
Outdoor						
Home	No	0.5	0	0		
ATM-Bank	Yes	0.2	0.097 (b)	0.019		
Airport	Yes	1	0.72 (c)	0.72		
Dining	Yes	1	0.19 (d)	0.19		
Other	No	1	0	0		
Total Outdoor		**3.7**		**0.929**	**2.9**	**0.25**
Total =		**24**		**32** (e)	**100**	**1.33**

a) From Seigel *et al*., 2003, the mean of average nicotine values reported in individual U.S. studies weighted by the number of establishments sampled in each study. This mean is considered an upper bound for an assumed level of nicotine for bars in this exposure scenario, because the estimate is based in part on data obtained from older studies of bars where smoking was allowed, and smoke would have been more concentrated than it would be in non-compliant California bars.
b) The mean 1-hour average concentration in a Local Government Office Building Complex Outdoor Smoking Area is used at input, assuming a low number of cigarettes smoked near the ATM.
c) The mean 1-hour average Airport Terminal concentration.
d) The mean 1-hour average Public Office Building Complex Outdoor Smoking Area.
e) Total may not add exactly due to rounding to significant figures.

The results for the business traveler spending time in a non-compliant bar indicate that by far the major exposure of this nonsmoking traveler would occur in the non-compliant bar. Non-smoking business travelers travelling with smoking co-workers or working with smoking clients would likely be exposed to higher levels of ETS, on average, to the extent that they visit smoking environments that they would not otherwise visit.

4. Summary and Conclusions

Table V-11 below summarizes the results of all of the exposure scenario calculations. The total 24-hour air exposure for the individuals represented in each scenario is

presented, along with the 24-hour average air concentration that such an exposure represents. The total indoor exposure for each scenario and the ratio of the total indoor exposure to the total exposure (indoor plus outdoor) is also provided.

Table V-11

Summary of Nicotine Exposure Scenario Results

Exposure Scenario	Total 24-hour Air Exposure (time-integrated exposure) (µg-hr/m^3)	Total Indoor Exposure (µg-hr/m^3)	Percent Contribution of Indoor Exposure to the Total Exposure (%)	Average 24-hour Air Concentration (time-weighted exposure) (µg/m^3)
C1 – Children's Low	0.24	0	0	0.010
C2 – Children's Medium	39	38	99	1.6
C3 – Children's High	77	72	94	3.2
C4 – Children's Maximally Exposed	81	72	89	3.4
S1 – College Student's Low	0.10	0	0	0.0043
S2 – College Student's High	49	48	98	2.0
T1 – Business Traveler	1.1	0	0	0.047
T2 – Business Traveler – Bar	32	31	97	1.3

The results of the scenario calculations show a wide range of possible exposures in the subgroups of the population for which exposure scenarios were developed. For individuals living in non-smoking homes and having only very brief encounters with ETS, exposures are very low, about 1µg-hr/m^3 . Some individuals in the population would be expected to have near-zero exposures, if their activity patterns do not bring them near smokers other than on rare occasions. However, the primary, and often the only, exposure for those individuals occurs outdoors in locations over which the individual typically has little control. For non-smokers whose work or other activities bring them into contact with outdoor smokers regularly, 100% of their exposure can be attributable to proximity to outdoor smoking.

Nonsmokers who visit non-compliant bars with smoking business associates, clients, or friends likely experience relatively high exposures to ETS; however, compliance with California's workplace restrictions in free-standing bars is increasing by almost 8% a year (Weber *et al*., 2003), so within a few years it is likely that nearly all bars in California will be compliant.

For those living in homes with smokers, indoor and in-vehicle exposures are predominant and high, as would be expected, ranging up to 81 μg-hr/m^3 , and potentially even higher in the actual population. These high exposures are due in part to the time spent in those locations as well as to the number of cigarettes typically smoked there and the trapping effect of enclosed environments such as apartments and cars. Such exposures are especially of concern for young children, both because they are likely to recur daily and because of the potential additional physiological sensitivity of developing children.

Conclusions:

- Exposures to ETS are highly variable in California.

- Outdoor smoking appears to be the key source of exposure for individuals who live in non-smoking homes in California, based on the prohibition of smoking in indoor workplaces and illustration by the scenarios above.

- Outdoor smoking can contribute from near zero to 100% of an individuals' exposures to ETS.

- Indoor exposures contribute most to exposure for those living in homes with smokers. Children living with smokers are especially likely to be impacted, since they spend a large portion of their time inside the home and in other locations where the smoking parent or guardian spend time, such as outdoors at home and in the family car.

F. BIOLOGICAL MARKERS OF EXPOSURE TO ETS

1. Introduction

This section addresses the use of biological markers (biomarkers) to measure ETS exposure. Information from the 1997 Cal/EPA report: *Health Effects of Exposure to Environmental Tobacco Smoke* was used as a starting point for the development of this section. The 1997 Cal/EPA report presented a great deal of information on the philosophy behind and rationale for using biologic markers of tobacco smoke exposure. Concentrations in physiologic fluids of adults, comparisons of levels in smokers, ETS-exposed non-smokers, and unexposed non-smokers, and concentrations in physiologic fluids of infants and children, in breast milk and amniotic fluid were described. The use of levels of exhaled carbon monoxide and blood levels of carboxyhemoglobin, as well as thiocyanate levels in blood, urine and saliva as biomarkers of ETS exposure were also addressed, as were DNA and protein adducts and other approaches of assessing tobacco smoke exposure. This updated section generally presents a combination of relevant older data and new studies as a single coherent document rather than separating the findings of the previous report. Where appropriate, discussions on previous findings are either included within sections or presented in the opening paragraphs. The major updates to information presented in the 1997 OEHHA report are highlighted below.

New studies presented in the update to this section strongly reinforce the findings in the 1997 Cal/EPA report regarding physiologic fluid levels of cotinine in adults, as well as the strong dose-response relationship between levels of this metabolite and ETS exposure. The results of recent large -scale studies provide useful correlations between daily cigarette exposures and cotinine levels. Similar studies using personal exposure monitors provide a link to average ETS atmospheric concentration and physiologic cotinine levels. Improved laboratory techniques are described with levels of detection sufficiently low that non-exposed non-smokers can be distinguished based on cotinine levels from persons with low exposure levels. Most studies presented in the 1997 Cal/EPA report did not have low enough levels of detection to do this. New studies also reinforce previous findings regarding appropriate cutoff cotinine levels to distinguish between smokers and non-smokers.

New to the biomarkers discussion is the use of hair nicotine levels as a useful biomarker of exposure. This science is still in its infancy, but results thus far indicate that hair nicotine is more useful in characterizing long-term exposure to ETS than cotinine.

The children studies presented in the 1997 Cal/EPA report address cotinine and nicotine levels in physiologic fluids of infants and children as well as in amniotic fluid and breast milk. The update reinforces the previous findings, while adding new light on half-lives of cotinine both in normal children and asthmatics. Recent studies also better characterize exposure patterns in infants and children based upon cotinine levels. New with this update is information on other biomarkers of ETS exposure in children, including carcinogenic nitroso compounds, thiocyanate and protein adducts.

Recent work using other biomarkers such as thiocyanate reinforced the lack of specificity found in the 1997 Cal/EPA report. DNA and protein adducts of tobacco specific metabolites are generally not useful in distinguishing between non-smokers and passive smokers, a finding that is also consistent with the 1997 Cal/EPA report.

Introductory subsections of this section are basically unchanged from the 1997 Cal/EPA report. These subsections describe the basic science behind the use of biomarkers, and little has changed in this area.

2. Introduction to Biomarkers of ETS Exposure

Measured biological parameters, such as the concentrations of metabolites, signaling compounds or tissue constituents, may be used as indices of either the extent of exposure to an external stimulus, such as a toxic environmental contaminant (biomarkers of exposure), or of the extent of a specific response to such as stimulus, including biochemical or histological damage, altered physiology, *etc.* (biomarkers of effect). The current section examines the utility of biomarkers specifically to assess the extent of exposure to ETS. This can be assessed directly by the analysis of physiologic fluids (urine, saliva, and serum) or human hair for tobacco smoke constituents or their metabolites. Nicotine, cotinine, thiocyanate, carboxyhemoglobin, hydroxyproline, N-nitrosoproline, aromatic amines, and certain protein and DNA adducts have been used as indicators of exposure to tobacco smoke. With the exception of the DNA adduct measurements, which may for some purposes be regarded as an early-stage biomarker of adverse genotoxic effects, these biomarkers do not indicate the presence of, or susceptibility to, disease due to exposure to tobacco smoke. Rather, these biomarkers simply reflect that the individual has been exposed to tobacco smoke. While few of the biomarkers listed above are entirely specific to tobacco smoke, when other known sources are accounted for, the presence of these marker compounds in tissues or body fluids can be attributed to smoke exposure. The appropriateness of a given biomarker depends on the nature of the study and the type of exposure being assessed (e.g. recent or long-term).

The relationship between a biomarker and exposure is complex, and varies as a function of both environmental and physiologic factors. The degree of exposure is a function of the time an individual spends in each setting and the air concentration of tobacco smoke constituents in that environment. Factors affecting air concentrations include smoking intensity, room size, room ventilation, and the furnishings and construction materials of the room. For a given air concentration, several factors will affect an individual's intake, such as gender, age, weight, and activity level (and corresponding inhalation rate) at the time of exposure. In addition, individual differences in uptake, distribution, and metabolism will affect the concentration of the indicator compound in tissues or body fluids. Racial differences in metabolism may also affect the biomarker concentration. Caraballo *et al.* (1998) review of the NHANES III data, found among smokers that African Americans had substantially higher cotinine concentrations than did whites or Hispanics at all levels of cigarette consumption. While the presence of a biomarker indicates that tobacco smoke exposure has occurred, and a given individual will show a positive association between ETS exposure and

biomarker levels, biomarker concentrations across individuals correlate only approximately with the amount of exposure to tobacco smoke. The atmospheric lifetime of a biomarker must also be considered when designing a study that attempts to characterize long-term exposure.

a) Biomarkers: Nicotine and Cotinine

i) Nicotine and Cotinine: General methodological issues

Cotinine, the major metabolite of nicotine, has emerged over the past 20 years as the biomarker of choice for most field exposure studies and for validation of smoking status. The update to the 1997 Cal/EPA report primarily focuses on the new data from large epidemiologic studies relating cotinine in body fluids to levels of second hand smoke exposure. Many small scale studies linking cotinine levels to ETS exposure have been done over the last decade that are not mentioned simply because the results echo those of the larger studies.

In general, the presence of nicotine or its metabolites in physiological fluids can be attributed to exposure to tobacco smoke. The few exceptions include occupational exposure to tobacco leaves and nicotine products, use of smokeless tobacco products, chewing of nicotine gum, and use of nicotine patches or other smoking cessation aides. Low levels of nicotine have been found in tea and in edible solanaceous plants including eggplant, green pepper and tomato, but these sources are not considered to be significant in comparison to tobacco sources (see 1997 Cal/EPA report; Tunstall-Pedoe *et al*. (1991); Pirkle *et al*. (1996)).

As biomarkers of exposure, nicotine and/or cotinine concentrations are typically measured in blood, saliva or urine. Quantitative assessment of exposure has been done using all three fluids. Recent work by Bernert *et al*. (2000), using sensitive laboratory techniques, indicate that salivary and serum cotinine levels are approximately equal, where it had previously been felt that the salivary glands tend to concentrate cotinine over serum by 20 – 40% (Curvall *et al*., 1990). The kidney concentrates cotinine, with urinary levels increased by a factor of 5 or 6 over serum (see 1997 Cal/EPA report; Benowitz NL, 1996; Peterson EL, 1997). Investigators over the last decade have also used nicotine in human hair as a biomarker for tobacco smoke exposure.

Urinary cotinine excretion is variable across and within individuals, depending on renal function, urinary flow rate and urinary pH (see 1997 Cal/EPA report). Urinary results may be expressed as nanograms of cotinine per milligram of creatinine in order to correct, in part, for differences in dilution effects. Because the amount of endogenous creatinine produced is a function of muscle mass, and hence, age and sex, individual excretion rates of creatinine are also variable. In particular, cotinine:creatinine ratios may not be appropriate for comparisions between males and females. In addition, low levels of creatinine in infants relative to adults may result in cotinine to creatinine ratios for infants that fall into the range reported for active smokers (see 1997 Cal/EPA report).

In general, it is preferable to collect urine over 24 hours, although it is impractical in most cases.

ii) Nicotine and Cotinine – Duration in body fluids/hair

The average half-life of cotinine in different body fluids (plasma, saliva, urine) is about the same, approximately 15 to 19 hours, making it a good indicator of the integrated ETS exposure over the previous two to three days. The half-life is typically longer in infants and children. While the half-life of cotinine has been well studied in adults, little data exists for infants and children. Etzel *et al.* (1985) found half-lives of approximately 68 hours in neonates with wide variability. The U.S. EPA lists half-lives of 60 hours in infants under 18 months and 40 hours in children over 18 months (U.S. EPA, 1992). Recent work, however, by Leong *et al.* (1998) found similar half-lives of about 27 and 28 hours (no statistical difference) between children under and over two years of age. They postulated that higher cotinine levels in infants are actually due to greater exposure rather than slower metabolism. Cotinine levels in children are discussed in much greater detail in subsection 6**.** Clearly, more work is needed in this area. Nicotine, with its shorter half-life of approximately two hours, is a good indicator of recent exposure.

Hair nicotine has recently been used as an indicator of longer-term exposure, on the order of months to years. Hair grows at approximately 1 cm per month, and nicotine deposited within the hair shaft is stable throughout the life of the hair. Nicotine is deposited in the hair shaft both systemically during the synthesis of the hair shaft and by uptake from atmospheric exposure. The contributions of nicotine to the hair shaft from these two processes is an area of debate. Mizuno *et al.* (1991) proposed that the dominant process is the systemic pathway based on a constant level of nicotine along the shaft in smokers and a downward gradient toward the root in persons that had quit smoking. They did not evaluate the atmospheric pathway. In contrast, Zahlsen and Nilsen (1990) reported such a gradient in both smokers and non-smokers. In addition, they and others report a large nicotine/cotinine ratio in hair of approximately 15:1 that is essentially the inverse of the ratio of these compounds found in bodily fluids. Hence, they postulated that absorption of nicotine from the atmosphere was the predominant pathway for uptake (Zahlsen and Nilsen, 1990, Nilsen *et al.*, 1994). Addressing this controversy, work done by Gerstenberg et al. (1995) on rat hair demonstrated that the processes are of the same order of magnitude, with up to ten-fold higher levels in pigmented versus unpigmented rat hair. The affinity of nicotine for melanin was noted also by Uematsu *et al*. (1995). More work in this area is clearly needed.

The value of hair nicotine as a biomarker for ETS exposure is less controversial. Zahlsen *et al*. (1996) found that hair nicotine levels tracked both smoking habits consistently among smokers and ETS exposure among non-smokers. Hair nicotine can distinguish between ETS exposed and non-exposed children, and was found to be a better indicator of level of exposure than urinary cotinine in children (Al-Delaimy AK *et al*., 2002; Al-Delaimy AK *et al.,* 2001; Nafstad *et al*., 1995). Pichini *et al*. (1997) found that hair nicotine levels in infants was consistent with exposure by questionnaire while serum cotinine levels were below detection limits. Hair nicotine has also been used as

a marker of gestational smoking (Eliopoulos *et al*., 1996), as a marker for compliance with smoking cessation (Uematsu *et al*., 1995).

3. Analytical Methods for Nicotine/Cotinine

Laboratory methods are available that accurately quantify nicotine and cotinine in body fluids or hair. Inter-laboratory studies outlined in the 1997 OEHHA report found that gas chromatography and radioimmunoassay techniques reliably quantify nicotine and cotinine in plasma and urine, and both techniques are capable of discriminating between smokers and non-smokers. High performance liquid chromatography and gas chromatography are the most specific, especially when combined with mass spectrometry (Haufroid and Lison, 1998) and both techniques have been widely used. Levels of detection for cotinine vary from as low as 0.05 ng/ml for gas chromatography/mass spectrometry to as high as 1.0 ng/ml (Phillips *et al*., 1999) for radioimmunoassay, depending on the methodology followed. The 1997 OEHHA report documents substantial inter-laboratory variability, with many laboratories unable to detect cotinine in exposed non-smokers. Addressing the need for greater analytical accuracy in exposed non-smokers, Phillips et. al. recently developed a chromatographic method utilizing tandem mass-spectrometry for detection of saliva cotinine with sufficient sensitivity to 0.05 ng/ml. This sensitivity will reliably distinguish between exposed and unexposed non-smokers (Phillips *et al*., 1999). Similar methods were used in the NHANES III Study (Caraballo *et al*. (1998)). Hair nicotine levels have been measured by radioimmunoassay techniques (Eliopoulos *et al*., 1996; Al-Delaimy *et al*., 2001) and also reliably differentiate between exposed and unexposed non-smokers (Al-Delaimy *et al*., 2001).

a) Cotinine Concentrations in Body Fluids

The levels of ETS encountered by exposed non-smokers during their daily activities are sufficiently high that nicotine and cotinine are detected in their urine, blood, saliva and hair. Given its longer half-life, high sensitivity, specificity and ease of measurement as a biomarker, cotinine rather than nicotine has emerged as the biomarker of choice for most ETS studies. Numerous studies are available that report concentrations of cotinine in the physiologic fluids of smokers and non-smokers. Because several recent, very large scale studies have published their results since the printing of the 1997 Cal/EPA report, the numerous smaller studies will not be discussed here, except to say that cotinine levels seen in these studies tend to agree with those discussed below.

The 1997 Cal/EPA report found cotinine levels in saliva and plasma of non-smokers typically in the range of 0.5 ng/ml to 15 ng/ml, and urinary concentrations as high as 50 ng/ml or even higher. The Health Survey for England, with over 20,000 participants, compared the plasma cotinine concentrations in non-smoking partners of smokers to partners of non-smokers. The study found that non-smokers in non-smoking homes had average plasma cotinine levels of 0.31 ng/ml, while non-smokers with partners smoking 30 or more cigarettes daily had an average plasma cotinine of 1.99 ng/ml. There was a very strong positive relationship between number of cigarettes smoked by

the partner and plasma cotinine levels in the non-smoker. Cotinine levels were also related to the partners cotinine levels, with plasma cotinine averaging 0.31 ng/ml when the partners cotinine was less than 15 ng/ml, and 1.30 ng/ml when the partners was over 4.0 ng/ml (Jarvis *et al.,* 2001). Analyzing data from the 16 City Study, LaKind *et al*. (1999), reported that non-smokers exposed to ETS in both the home and work environment had average salivary cotinine levels of 1.78 ng/ml, while unexposed non-smokers had cotinine levels averaging 0.182 ng/ml. Lee found a similar relationship between ETS exposure and serum cotinine. In four large scale studies listed in the review (over 18,000 subjects), average cotinine levels in non-exposed non-smokers was about 0.7 ng/ml, while in the most heavily exposed non-smokers the levels averaged about 2.5 ng/ml (Lee, 1999), which reinforces findings of the Health Survey of England fairly well. There are many smaller scale studies that reinforce these numbers. Urine concentrations of cotinine in 6 studies reviewed by Lee varied more widely, with some studies as low as 4.0 ng/ml and others as high as 680 ng/mg creatinine. Most studies show urine cotinine levels in non- smokers as less than 10 ng/ml or 10 mg/mg creatinine (see Table 8, Lee, 1999). The studies showing the higher values may not have removed subjects from the study that had cotinine values in the smoker range, so the higher number may not be truly reflective of non-smokers. Galanti *et al.* (1998) reported urinary cotinine concentrations among 2,431 young men in the Belgian Armed Forces averaging 32 ng/mg creatinine in non or ex-smokers and 717 ng/mg creatinine in active smokers. Criteria in this study for ex-smoker was no smoking within the last month.

Studies of individuals exposed in locations of exceptionally high concentrations of ETS provide some indication of the maximum concentrations of nicotine and cotinine reported in non-smokers. Jarvis *et al*. (1992), as described in the 1997 Cal/EPA report, reported a median salivary cotinine concentration of 7.95 ng/ml in 42 nonsmoking bar staff in England, with a maximum concentration of 31.3 ng/ml. Maskarinec *et al*. (2000) reinforced these findings in a similar population of bar staff. Using personal exposure monitors as described below, the highest salivary cotinine levels among bartenders (the 95th cotinine percentile) was as high as 20 ng/ml (see more on this study below). The 1997 Cal/EPA report describes a study of individuals exposed on commercial airline flights. The highest average urinary cotinine concentrations among those who were measured was approximately 30 ng/mg creatinine (Mattson *et al.,* 1989). A similar flight attendant study by Lindgren *et al*. (1999) measured urinary cotinine concentrations as high as 36 ng/mg creatinine, reinforcing the previous findings. Haufroid *et al*. (1998) asserts that urinary cotinine levels in non-smokers are always less than 100 ng/mg creatinine.

b) Relationship Between Cotinine Levels and Air Nicotine Levels by Personal Exposure Monitoring

The 1997 Cal/EPA report presented a study by Hoffmann *et al*. (1984) that linked air nicotine levels to salivary cotinine levels. Hoffmann evaluated salivary cotinine in a closed room with 10 non-smoking volunteers. ETS was generated via a smoking machine. At a nicotine air concentration of 280 µg/m^3, salivary nicotine levels reached an average of 880 ng/ml after 60 minutes of exposure, while cotinine climbed to 3.4

ng/ml 6 hours post exposure (1997 Cal/EPA report, Hoffmann *et al.,* 1984). Experiments such as these have been replaced by personal exposure monitoring, where the subject wears a monitor that collects air close to the subjects breathing zone for a set period of time. Air concentrations of nicotine, respirable particulate matter, ultraviolet-absorbing particulate matter, solanesol, scopoletin, and 3-ethenyl pyridine are typically measured. The metabolite of interest, typically cotinine, is analyzed at various times before, during and after the monitoring time frame. Such monitoring in theory gives an exposure picture that closely approximates day-to-day living.

As a prelude to the following studies, concerns have been raised regarding the validity of the findings regarding workplace and home exposure to ETS. A multitude of concerns regarding the 16 City Study are discussed in U.S. EPA, 1996. Among many concerns is the low nicotine concentrations measured in the workplaces, which are significantly lower than nicotine concentrations measured as area concentrations at worker's desks in similar studies (Hammond *et al*, 1999). Nicotine concentrations reported by Phillips *et al.* (1998) also are lower than in comparable studies (Phillips and Bentley (2001), or in area studies (Hammond *et al*., 1999). In presenting the data, the ARB is not endorsing findings regarding the contribution of the workplace versus the home environment to ETS exposure. Rather, we are simply presenting data linking physiologic cotinine levels to measured atmospheric nicotine levels.

Phillips *et al.* (1999) has performed personal exposure monitoring on over 1000 subjects in 8 European cities, 3 Asian cities and in Sydney, Australia. His data allow categorization of exposure into a number of environments, i.e. non-smoking work/ home, smoking work/ home, and combinations of these, depending on the study. Table V-12 presents the 24-hour time weighted average air concentrations of nicotine and salivary cotinine in European and Asian housewives.

Table V-12

Nicotine Concentrations in Inhaled Air with Corresponding Salivary Cotinine Concentrations

Location	Nicotine (µg/m3)		Cotinine (ng/ml)	
	SH	NSH	SH	NSH
Stockholm	1.1	<0.08	2.9	<1.0
Barcelona	0.74	0.11	1.4	<1.0
Turin	1.1	0.14	1.4	<1.0
Paris	0.52	0.13	1.3	<1.0
Bremen	0.49	<0.08	1.4	<1.0
Lisbon	0.19	<0.08	1.2	<1.0
Basel	0.6	<0.08	1.0	<1.0
Prague	0.72	0.15	1.2	<1.0
Hong Kong	<0.06	<0.06	<1.0	<1.0
Kuala Lumpur	0.18	<0.06	1.0	<1.0
Beijing	1.4	0.15	<1.0	<1.0
Sydney	0.3	<0.08	1.4	<1.0

SH: Smoking home, NSH: Non-smoking home.
Adapted from Phillips et al., 1999 – Table 1 and 2.

These data clearly demonstrates the increased cotinine in housewives of smoking versus non-smoking homes. Many of the cotinine values measured were near or below the limit of quantification for radioimmunoassay, hence stronger trends were unable to be derived. Variations in home nicotine levels are strongly influenced by season and climate, i.e. ventillation.

Phillips *et al*. (1998) looked at subgroups based on lifestyle in some studies. In Prague, subjects were divided into 6 lifestyle groups (Table V-13).

Table V-13

Effect of Home Versus Work Smoking Environment on Exposure to ETS

Cell	Home Environment	Work Environment	Arithmetic mean cotinine (ng/ml)	Arithmetic mean nicotine (µg/m3)
1	Smoking	[a] -	2.4	1.3
2	Non-smoking	[a] -	0.98	0.31
3	Smoking	Smoking	2.7	2.3
4	Smoking	Non-smoking	1.9	1.3
5	Non-smoking	Smoking	1.4	1.1
6	Non-smoking	Non-smoking	0.71	0.25

Adapted from Phillips *et al*., 1998.
(All subjects had cotinine < 25 ng/ml).
a - implies non-working

These data further reinforce the relationship between ETS exposure and cotinine levels discussed previously. The data also demonstrates that home environment as a greater contributor to ETS exposure than the work environment. Workplace nicotine levels in this study are lower than those measured in other similar studies (please see Table V-9).

A different subgroup analysis was done by Phillips *et al*. (2001) in Bremen. Nicotine and cotinine were averaged over 24 hours and 7 days during both winter and summer on people either living and working in smoking locations or living and working in non-smoking locations (Table V-14).

Table V-14

Seasonal Effect on ETS Exposure

Cell	Locations	Length of monitoring	Arithmetic mean cotinine (ng/ml)	Arithmetic mean nicotine (µg/m3)
1	Smoking	24 hour –winter	1.6	2.7
2	Smoking	7 day – winter	1.6	2.1
3	Smoking	24 hour-summer	0.94	1.1
4	Smoking	7 day-summer	0.76	1.6
5	Non-smoking	24 hour –winter	0.73	0.36
6	Non-smoking	7 day – winter	1.2	0.27
7	Non-smoking	24 hour-summer	0.56	0.11
8	Non-smoking	7 day-summer	0.55	0.05

Adapted from Phillips *et al*., 2001.
(All subjects had cotinine < 25 ng/ml).

Once again, these data demonstrate close relationship between ETS exposure and cotinine, as well as the importance of ventillation on ETS exposure.

In the 16 City Study referenced above, similar to Phillips *et al*., La Kind *et al*. (1999) analyzed personal exposure on over 1000 subjects in 16 American cities. La Kind *et al*. (1999) divided subjects into 4 cells and found the following results (Table V-15):

Table V-15

Effect of Home Versus Work Smoking Environment on Exposure to ETS

Cell	Home Environment	Work Environment	Median cotinine (ng/ml)	Median nicotine (µg/m3)
1	Smoking	Smoking	1.78	1.55
2	Smoking	Non-smoking	0.807	0.49
3	Non-smoking	Smoking	0.347	0.11
4	Non-smoking	Non-smoking	0.182	0.03

(All subjects had cotinine < 15 ng/ml).

Similar to Phillips *et al*. (1998), they concluded that the home environment was more significant in terms of exposure than the work environment. Once again, the validity of the workplace nicotine levels has been challenged (U.S. EPA, 1996). Limited information on cotinine concentrations in California subjects is available. In the 16 City Study by Jenkins *et al*. (1996), Fresno, CA was the only California region evaluated. Atmospheric nicotine concentrations both at work and away from work were among the lowest of the cities tested. These low concentrations contrast with data from an earlier, large multinational study which included a center located in Los Angeles (Riboli *et al*., 1990). Riboli *et al*. studied 100 non-smoking women with the following marital and employment status: 13% married to a smoker and employed; 39% married to a smoker and unemployed; 16% not married to a smoker and employed; and 32% not married to a smoker and unemployed. The mean urinary cotinine/creatinine ratio was approximately 8.5 ng/mg for the entire population, and 10.5 ng/mg for those with detectable urinary concentrations. The differences in cotinine levels were found to be large and statistically significant between the 13 centers, and the concentrations at the Los Angeles center was one of the three highest of the centers in the study.

c) Nicotine and Cotinine: Comparison of Levels in Smokers, and ETS-exposed and Unexposed Non-smokers

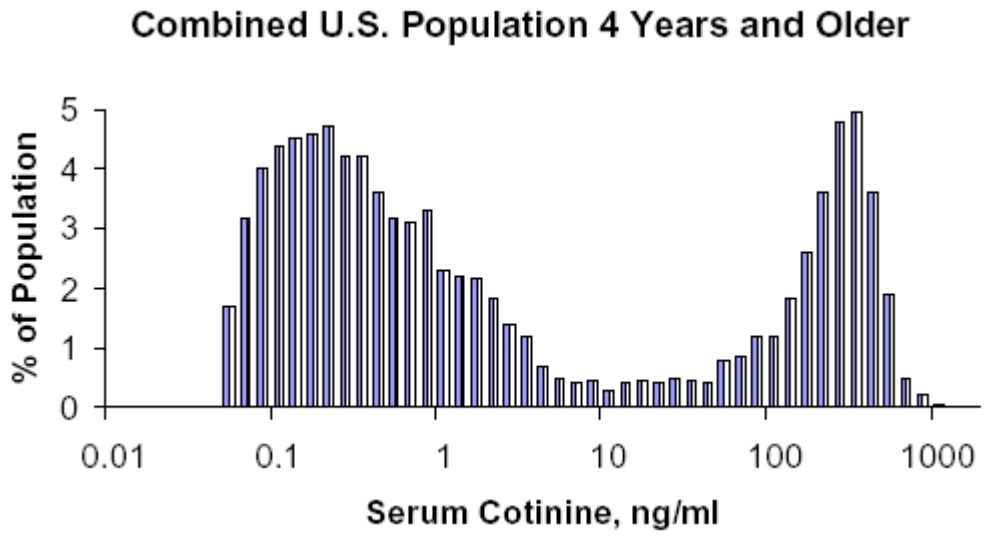
Cotinine assays using serum, saliva or urine can consistently distinguish between smokers and non-smokers. Ogden *et al.* (1997), in a nationwide survey, found the mean salivary cotinine in active smokers to be 352.9 ng/ml. Findings from this study and the 1997 Cal/EPA report consistently show at least an order of magnitude difference in the cotinine concentrations between active and non-smokers. Data below also graphically depict this difference. Findings in the 1997 Cal/EPA report, though, were less consistent with regard to distinguishing between ETS exposed and unexposed non-smokers, for reasons including limited analytical accuracy, misreporting

of exposure, variations in metabolism and others. The more recent large studies, using sensitive analytical methods such as HPLC, have been consistently able to distinguish between ETS-exposed and unexposed non-smokers.

The relationship between ETS exposure and cotinine is clearly demonstrated in Figures V-1 through V-3 which present data from the very large NHANES III study and the Health Survey for England. Figure V-1 (Pirkle *et al*., 1996) below presents serum cotinine levels in over 10,000 participants in the NHANES III study.

Figure V-1

Distribution of Serum Cotinine Levels in the US Population Aged 4 Years and Older

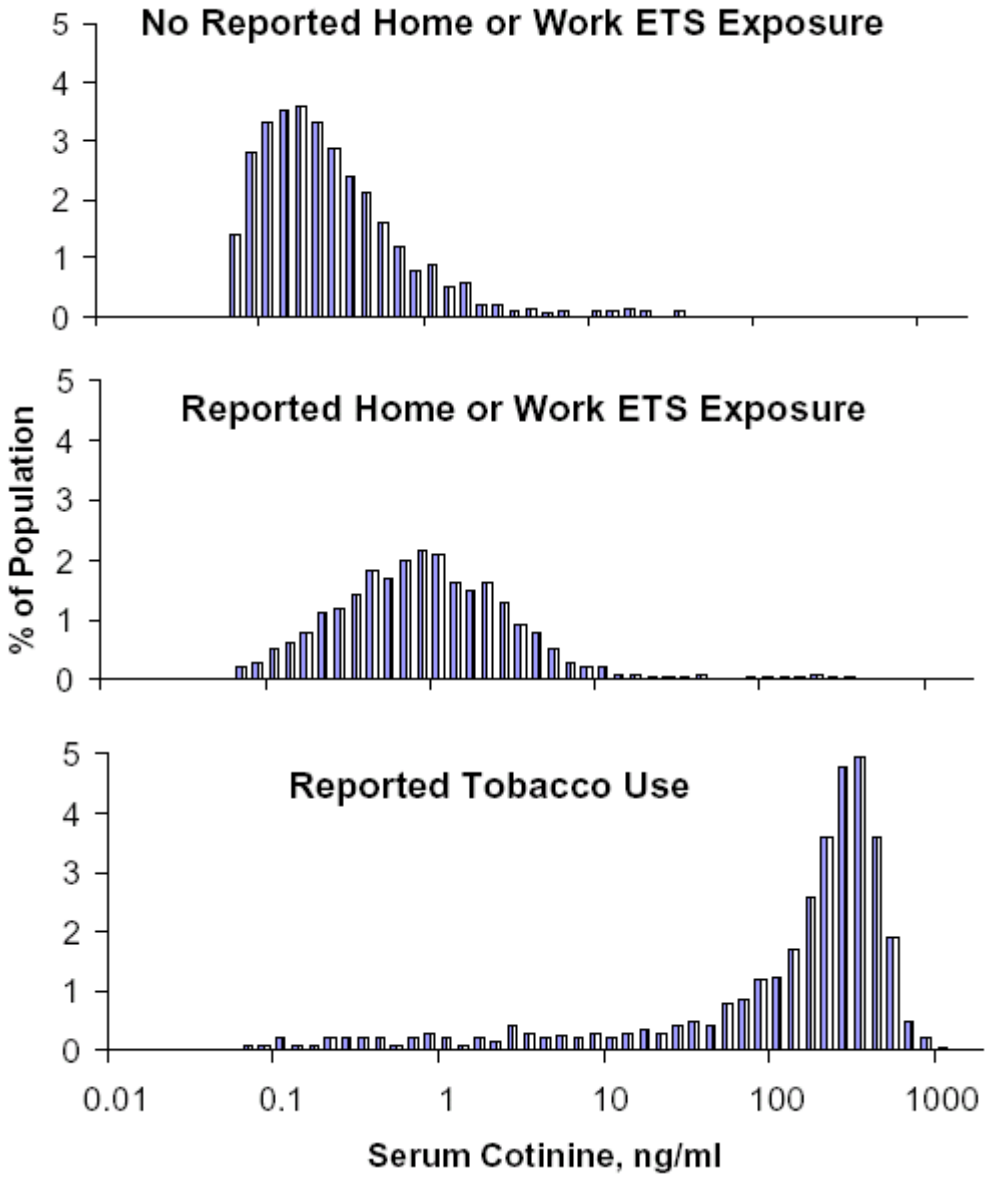


Distribution of serum cotinine levels in the US population aged 4 years and older: Third National Health and Nutrition Survey, October 25, 1988, to October 21, 1991. **Source: Pirkle *et al*., 1996**.

Figure V-2 (Pirkle *et al*., 1996) divides this data into groups based on type of exposure.

Figure V-2

Distribution of Serum Cotinine Levels in the US Population Aged 4 Years and Older by Tobacco Use

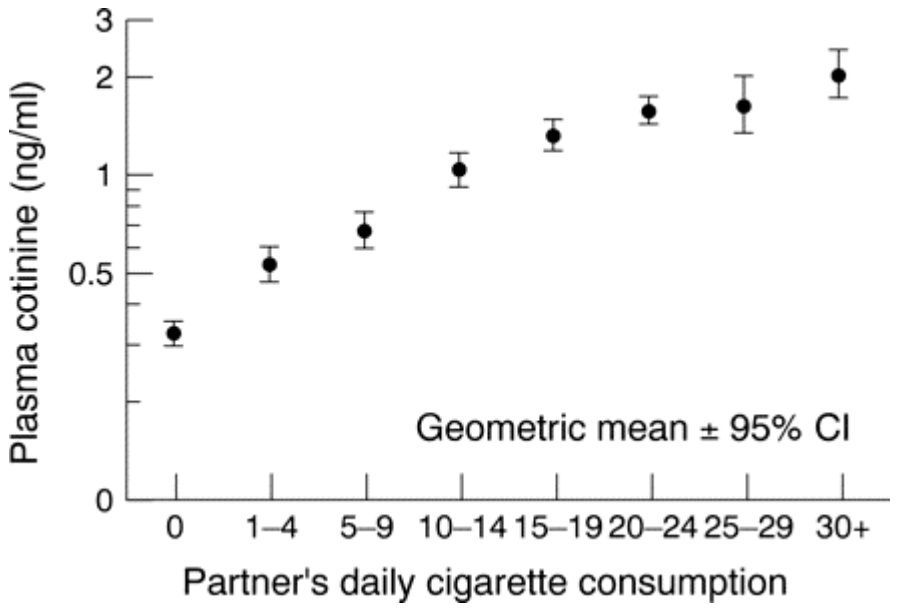


Distribution of cotinine levels in the US population aged 4 years and older by reported environmental tobacco smoke exposure and tobacco use: Third National Health and Nutrition Examination Survey, October 25, 1988, to October 21, 1991**. Source: Pirkle *et al*., 1996**.

The bimodal distribution depicted above has been demonstrated in other studies. The lower hump represents non-smoking individuals exposed either in their work or home environment to environmental tobacco smoke. The higher cotinine hump represents active smokers. Those values between approximately 10 and 25 ng/ml of cotinine represent an area of uncertainty as to whether these individuals are heavily exposed non-smokers or occasional smokers. The curve below, derived from the Health Survey of England (Jarvis *et al*., 2001) provides a detailed look at the cotinine concentrations in over 20,000 partners' of smokers based on the partners' cigarette consumption.

Figure V-3

Cotinine Concentrations Based on Cigarette Consumption



Source: Jarvis *et al*., 2001

The power of these studies provides strong evidence that cotinine levels in non-smokers are almost always below 10 ng/ml. These data are well supported by numerous studies in the past (see 1997 Cal/EPA report, review by Lee, Phillips *et al.* (1999)). Pregnant women with similar ETS exposure will have lower cotinine levels than non-pregnant subjects due to higher renal clearance rates (see reproductive health effects in Part B of this report). Authors usually list their cutoff level at which they designate a subject as a non-smoker, with almost all authors opting for a cutoff between 10 and 25 ng/ml. Caraballo *et al.* (1998), in reviewing the NHANES III data, found that a serum or plasma cotinine level below 15 ng/ml is consistent 98 – 99 percent of the time with non-smoking status. Maskarinec *et al*. (2000**)**, evaluating 173 non-smoking bar staff using personal exposure monitors in Knoxville, Tennessee, present cotinine levels from a small subset of the population with maximal ETS exposure (Table V-16).

Table V-16

Job-Related Cotinine and Nicotine Measured Concentrations

Home Status	Job Classification		Average Salivary Cotinine (ng/ml)	Shift Average Nicotine Concentration (µg/m3)
Smoking	Wait Staff	Median	4.08	3.20
		Mean	4.32	12.1
		80th percentile	6.05	17.8
		95th percentile	11.1	54.0
	Bartenders	Median	4.85	12.6
		Mean	6.54	19.2
		80th percentile	8.97	33.2
		95th percentile	20.2	57.9
Non-Smoking	Wait Staff	Median	1.43	0.93
		Mean	2.61	3.32
		80th percentile	3.62	4.47
		95th percentile	8.24	18.2
	Bartenders	Median	2.00	3.90
		Mean	3.67	11.2
		80th percentile	4.90	20.1
		95th percentile	12.8	34.9

Adapted from **Maskarinec *et al*., 2000.**

These data are not inconsistent with the findings of the larger studies discussed above. Rather, the high cotinine levels found in this study are consistent with those persons in the maximum ETS exposure percentile.

Etzal *et al*. (1990) proposed the following range:

Salivary Cotinine Level	**Smoking Classification**
<5 ng/ml	Passive smoking
>= 10 ng/ml	Heavy passive smoking
10 – 100 ng/ml	Infrequent to regular smoking with low nicotine content
>100 ng/ml	Regular active smoking

These ranges are consistent with data from the later, larger studies mentioned above.

4. Biomarkers: Carbon Monoxide and Carboxyhemoglobin

Carbon monoxide, both in exhaled alveolar air and as carboxyhemoglobin in blood, originates from endogenous processes as well as from environmental sources. In addition to cigarette smoke, common environmental sources include vehicle exhaust, gas stoves and furnaces, and kerosene space heaters. Although carbon monoxide and carboxyhemoglobin have been used to distinguish smokers from non-smokers (1997 Cal/EPA report), they are generally not good indicators of ETS exposure because of their lack of sensitivity and specificity. In non-smokers exposed to environments heavily polluted with ETS, elevated levels of exhaled carbon monoxide and carboxyhemoglobin in blood have been detected when measured 30 minutes following cessation of exposure. However, the use of these biomarkers in distinguishing between subjects with no, little or high levels of ETS exposures is limited (1997 Cal/EPA report).

5. Biomarkers: Thiocyanate

Present in the vapor phase of tobacco smoke, hydrogen cyanide is metabolized in the liver, yielding thiocyanate (SCN-). Thiocyanate levels in blood, urine and saliva have been used to distinguish smokers from non-smokers, or in combination with assays for nicotine or cotinine, to distinguish smokers from individuals using smokeless tobacco or nicotine-containing products (1997 Cal/EPA report). Sources of thiocyanate are also present in the diet, particularly cruciferous vegetables; thus, levels of thiocyanate in body fluids are not specific to exposure to tobacco smoke. In studies examining the use of thiocyanate as a biomarker of ETS exposure, it was not possible to distinguish between ETS-exposed and unexposed non-smokers (1997 Cal/EPA report). Recent work by Scherer *et al*. (2000**)** reinforces these previous findings. In the study described in subsection 6, non-exposed non-smokers had average plasma levels of thiocyanate of 22.0 µmol/L, which is higher, though not significantly different, than the corresponding level in ETS exposed non-smokers of 19.6 µmol/L. These same subjects had cotinine levels of 0.71 and 1.32 ng/ml, respectively, which are consistent with findings described in section 2(c) of this report. For this reason, thiocyanate is not very useful as a biomarker of ETS and has not been widely used for monitoring ETS exposure.

6. Biomarkers: Protein and DNA Adducts

Protein and DNA adducts represent both markers of exposure and measures of a biochemical effect. The 1997 Cal/EPA report found associations between levels of these adducts and cotinine, but no studies were presented linking their levels to quantitative ETS exposure. New studies using hemoglobin and albumin adducts describe significant overlap in the levels between unexposed persons and passive smokers.

One of the more common protein adducts measured is the hemoglobin adduct of 4-aminobiphenyl. Tobacco smoke is the primary source of environmental

4-aminobiphenyl. Because of the relatively long half-life of these adducts, their levels reflect exposures occurring over the previous 4 months. Levels of 4-aminobiphenyl in ETS-exposed non-smokers compared to those of active smokers present an interesting contrast to cotinine levels measured in these two groups. The levels of 4-aminobiphenyl adducts in non-smokers are approximately 10% to 20% of the levels measured in smokers. Although this finding appears to be inconsistent with the results for urinary cotinine, for which levels in ETS-exposed non-smokers are about 1% of those in smokers, the results may be explained by the available information on the relative levels of nicotine and 4-aminobiphenyl in mainstream and sidestream smoke (see U.S. EPA, 1992: Table 3-1). Approximately twice as much nicotine is present in sidestream as in mainstream smoke, whereas about 31 times as much 4-aminobiphenyl is present in sidestream as in mainstream smoke. As a result, the smoker/non-smoker ratio for 4-aminobiphenyl is about 15 times higher than for cotinine.

Another group of protein adducts which have been measured are the albumin adducts of polycyclic aromatic hydrocarbons (PAHs). Multiple PAHs are present in tobacco smoke. Crawford *et al.* (1994) analyzed PAH-albumin levels in peripheral blood of 87 mothers and their preschool children (2-5 years of age). They found PAH-albumin levels were significantly higher in the children whose mothers smoked than in the children of non-smoking mothers ($P<0.05$). Among the nonsmoking mothers, regression of PAH-albumin against total ETS exposure also showed a significant association with cotinine ($r^2=0.25$, $P=0.04$).

Scherer *et al*. (2000) performed biomonitoring of exposure to PAH's in a field study of 69 subjects using benzo[a]pyrene (a PAH present in tobacco smoke) adducts of hemoglobin and albumin as well as urinary 1-hydroxypyrene. Subjects were non-occupationally exposed to PAH's, and the non-smokers wore personal exposure monitors to quantify their exposure to ETS. Statistically significant differences in urinary excretion of hydroxypyrene and benzo[a]pyrene adducts were seen between smokers and non-smokers, but no significant differences were seen between ETS-exposed and non-exposed non-smokers.

Hemoglobin adducts of 4-hydroxy-1-(3-pyridyl)-1-butanone (HPB) have been studied by Atawodi *et al*. (1998) and others. In 70 hospitalized patients, hemoglobin-HPB adduct levels in 18 smokers averaged 26 fmol/g HB versus 19 fmol/g HB in 52 never smokers ($P=0.02$) (Atawodi *et al.,* 1998). No significant difference was seen between current smokers and ex-smokers. Carmella *et al*. (1990) reported levels of Hb-HPB in 40 smokers averaged 80 fmol/g Hb and 21 non-smokers averaged 29 fmol/g Hb, with large heterogeneity for both smokers and non-smokers**.** Foiles *et al*. (1992) reported averages in 100 smokers of 163 fmol/g HB and 68 fmol/g Hb in 37 non-smokers. Falter *et al.* (1994) reported averages of 69 fmol/g Hb and 34 fmol/g Hb for these same respective groups.

Bono *et al*. (1999) looked at levels of N-(2-hydroxyethyl)valine (HOEtVal) on hemoglobin, an adduct formed from the reaction of ethylene oxide (in tobacco smoke) and valine residues on hemoglobin. Among 146 subjects, HOEtVal levels correlated well with the number of cigarettes smoked, and the difference between smokers and

non-smokers was significant. However, no significant difference in HOEtVal levels between passive smokers and non-smokers was seen.

DNA adducts of tobacco smoke constituents can also be measured. The distribution of DNA adducts of benzo[a]pyrene diol epoxide, the ultimate carcinogenic metabolite of benzo[a]pyrene, has been analyzed by Denissenko *et al.* (1996**)** in the P53 tumor suppressor gene. These authors reported that exposure of human bronchial epithelial cells to benzo[a]pyrene diol epoxide resulted in strong and selective DNA adduct formation within the p53 gene at mutational hotspots identified in non-radon associated human lung cancer tissues obtained from smokers. This mapping of DNA adduct formation to mutational hotspots provides a direct etiologic link between a specific tobacco smoke carcinogen and human cancer. PAH-DNA adducts have been noted in smokers in many other studies.

7. Biomarkers: Other

Biomarkers of ETS exposure with high specificity for tobacco smoke include the metabolites of 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK). NNK is found only in tobacco products, therefore, its metabolites, 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol (NNAL) and its glucuronide (NNAL-Gluc), are specific to tobacco exposure. Hecht (2002) evaluated 16 carcinogen metabolites that appear in the urine following tobacco exposure for their utility as biomarkers. Among the compounds evaluated in addition to NNAL and its glucuronide (NNAL-Gluc) were nitrosamines, PAHs, mercapturic acids, benzo[a]pyrenes and naphthols. Of these, NNAL plus NNAL-Gluc showed the highest specificity for tobacco exposure and the best ability to differentiate those with and without ETS exposure. Hecht *et al*. (2001) demonstrated the utility of this biomarker in a study of ETS exposure in children described below (Section 8b).

Taniguchi *et al.* (1999) studied urinary levels of trans, trans-muconic acid, a metabolite of benzene and sorbic acid, in both passive smokers and active smokers. There was significant overlap between the light active smoker group and non-smokers exposed to ETS. Ruppert *et al*. (1997) also studied the urinary excretion of this compound. There was no significant difference in urinary levels between non-smokers living in smoking homes and those living in non-smoking homes. Hence, the usefulness of this compound as a biomarker is probably limited, particularly in view of the ubiquitous presence of benzene in ambient air from fuels.

8. Biomarkers and Children

a) Nicotine and Cotinine: Studies in Infants and Children

ETS exposure among infants and children was described in the 1997 Cal/EPA report. It is addressed here as a separate subsection to reflect the unusual exposure scenario associated with *in utero* exposure, and the involvement of two metabolizing systems, maternal and fetal, in affecting and affected by levels of nicotine and cotinine. Infants can be exposed prenatally to tobacco smoke constituents if the mother smokes or if the

mother is exposed to ETS during pregnancy. Postnatal ETS exposure may occur directly, via inhalation, and indirectly, from ingestion of breast milk.

Cotinine has been detected in fetal fluids as early as 7 weeks gestation in both active and passive smokers (Jauniaux *et al*., 1999). In a study of 85 pregnant women, cotinine levels above 25 ng/ml in maternal serum and above 250 ng/ml in maternal urine were associated with detectable cotinine levels in amniotic and coelomic fluids, and fetal serum. In active smokers, positive linear correlations were reported between maternal urine and amniotic fluid cotinine concentration, between maternal urine cotinine concentration and number of cigarettes smoked per day, and between maternal and fetal serum cotinine concentrations. Nafstad *et al*. (1996) measured cotinine in cord serum and found a significant correlation between the average number of cigarettes smoked by mothers and the concentrations of cotinine in cord serum. Using linear regression analysis of data from daily smokers, the reported increase in the concentration of cotinine in cord serum per daily cigarette smoked was 4.4 ng/ml.

In infants and children, nicotine and cotinine have been measured in hair, serum, saliva, and urine. Consistent with earlier reports, recent studies have shown that in children who are exposed to smoke, cotinine levels are associated with the age of the child, with the highest concentrations found in younger children. Irvine *et al*. (1997) studied children 2 to 12 years old, from 501 families with at least one parent who smoked. They reported a stepwise reduction in salivary cotinine levels with ascending age, with the largest reduction detected between the preschool four year olds and children ages 5 to 7 years. Similarly, Preston *et al.* (1997) reported that in a group 175 children ages 2 to 11 years, there were statistically significant differences in cotinine concentrations between age groups, with the highest concentrations of urine cotinine found in the youngest children (2 to 4 years) and the lowest concentrations in the oldest children (8 to 11). They also reported that children ages 2 to 4 years, with smoke exposure exceeding 1 pack per day, had mean cotinine levels almost two-fold greater than older children having similar exposures. Kohler *et al*. (1999) examined passive smoke exposure in children 1 month to 11 years of age. In this study, children were considered passive smokers if their urine nicotine metabolite concentration (i.e., cotinine plus OH-cotinine) was greater than 10 nmol/L. In addition to finding the highest concentrations in the youngest children, they also found that younger children ($\leq$ 5 years) were identified as passive smokers more frequently than children over 5 years (83.7% vs. 52.4%, $p < 0.001$). Mannino *et al*. (2001) also found age to be an important factor. They analyzed NHANES III data (i.e., data collected in 1994 as part of the United States' Third National Health and Nutrition Examination Survey) from over 5500 children, ages 4 to 16 years. Their analysis showed that age was an important predictor of serum cotinine levels both in children exposed to smoke and in those not exposed to smoke, although the effects were opposite in these two groups. In children exposed to smoke, the highest levels of cotinine were found in the youngest children while in the unexposed group, older children appeared to have higher cotinine levels, presumably from sources outside the home.

Several researchers have suggested that the higher concentrations of cotinine found in infants and younger children exposed to ETS are likely due to greater exposure, or a

higher relative dose of nicotine, rather than slower cotinine metabolism (Willers *et al*., 1995; Leong *et al.,* 1998; Mannino *et al*., 2001). Infants have a higher ventilation rate than older children or adults. It is also possible that they spend less time outdoors than older children, and/or since they are less mobile they are not able to leave a smokey environment. While the half-life of cotinine has been well studied in adults, little data exists for infants and children. Etzel *et al*. (1985) reported an average cotinine half-life in neonates of 68 hours, with a range of 37 to 160 hours, which is greater than that reported in adults. More recent findings, however, indicate there is no difference in half-life between infants and older children, or adults. Leong *et al*. (1998) reported no significant difference in the half-life of cotinine in children under two years of age compared to older children. In this study, the urinary elimination half-life of cotinine was measured in 31 infants and young children (mean age, 4.8 months; range, 0-22 months) and compared to that in 23 older children (mean age, 95.6 months; range, 39-174 months). The median half-life was approximately 28 hours in the younger group (range 6 – 259 hours), and 27 hours in older children (range 10 – 99 hours); this difference was not statistically significant. Similarly, Dempsey *et al.* (2000) found the half-life of cotinine in newborns to be consistent with what they had previously found in adults, reporting values in neonates of 16.3 hours in blood (95% CI = 12.4 to 23.9 hours) and 22.8 hours in urine (95% CI = 19.5 to 25.8 hours).

The Dempsey *et al.* (2000) study and the Etzel *et al.* (1985) study, while very similar in design (both collected urine samples from newborns during the first week of life), differed in that Dempsey did not normalize their data by creatinine concentrations, most likely accounting for the difference in the results of the two studies (Dempsey *et al.,* 2000). It is common to correct for the effect of hydration on the urine concentration of cotinine by adjusting the urine cotinine level for urine creatinine concentrations. Dempsey suggests that in neonates, however, adjusting for creatinine may lead to an overestimation of half-life. During the first week of life, neonates excrete a maternal load of creatinine, and therefore their urine creatinine concentrations do not reflect endogenous production. If this is true, then normalizing cotinine by urine creatinine concentrations leads to an underestimate of cotinine during the first few days of life, which would result in an overestimate of the cotinine half-life.

In addition to their work on cotinine, Dempsey *et al*. (2000) also measured half-lives of nicotine, 3´-hydroxycotinine and their conjugates. They reported that the half-life of nicotine in newborns is 11.2 hours in blood (95% CI = 8.0 to 18.9 hours) and 9 hours in urine (95% CI = 7.0 to 12.4 hours), which is three to four times longer than adults. The elimination half-lives for the other metabolites were 13 hours for conjugated nicotine, 19.8 hours for conjugated cotinine, 18.8 hours for 3´-hydroxycotinine, and 19.4 hours for conjugated 3´-hydroxycotinine.

Regardless of age, there are data to suggest that asthmatic children may have a lower clearance rate of ETS than nonasthmatic children. Klein and Koren (1999) compared concentrations of nicotine and cotinine in asthmatic and healthy (non-asthmatic) children (ages 2 to 18 years) exposed to similar degrees of ETS. Urine samples were collected from 71 asthmatic children and 81 controls, hair was collected from 64 asthmatics and 77 controls, and parents provided information regarding smoking in the

home. On average, the asthmatic children in this study were exposed to fewer cigarettes per day at home, although this difference was not statistically significant. Similarly, mean urine cotinine concentrations were lower in asthmatic children, although not statistically significant. In contrast, hair nicotine concentrations were almost twofold higher in asthmatic children compared to nonasthmatic controls ($p < 0.0001$), and the ratio of urine cotinine to hair cotinine was almost threefold lower in asthmatic children ($p < 0.0001$). Klein and Koren (1999) suggest that these data indicate a lower clearance rate of ETS in asthmatic children, and therefore a higher systemic exposure.

Mannino *et al.* (2001), who analyzed NHANES III data from over 5500 children across the U.S., found that the strongest predictor of cotinine levels in ETS-exposed children was the number of cigarettes smoked in the home. Studies have consistently shown that increased cotinine levels in ETS-exposed children are associated with the number of cigarettes smoked in the home, as well as the number of parents who smoke, particularly if mothers smoke (Irvine *et al*., 1997; Preston *et al*., 1997; Oddoze *et al*., 1999). Recent studies have also shown that, similar to adults, there are differences in cotinine levels among racial/ethnic groups. Mannino *et al.* (2001) reported the lowest mean cotinine levels among Mexican-American children, and the highest among black children in their study. Similar results were reported by Tang *et al.* (1999). The Tang study is discussed in greater detail below.

b. Other Biomarkers of ETS Exposure Measured in Children

In a study of elementary school-aged children, metabolites of the lung carcinogen 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK) were measured and quantified in urine (Hecht *et al*., 2001). NNK is found only in tobacco products; therefore, the metabolites 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol (NNAL) and its glucuronide (NNAL-Gluc) in urine are specific biomarkers of tobacco exposure. Two hundred and four children, grades 2-5, were included in this study (mean age = 8.9 yrs). Questionnaires were administered to caregivers about ETS exposure in the home. Urine samples from all of the children were analyzed for total cotinine (cotinine plus its glucuronide); a subset of 74 samples was also analyzed for the metabolites NNAL and NNAL-Gluc. Of the 204 children in the study, more than 34% had total cotinine levels $\geq$ 5 ng/ml urine, the cutoff used in this study to indicate ETS exposure. Among the samples with total cotinine $\geq$ 5 ng/ml, which were also analyzed for NNAL and NNAL-Gluc, 52 of 54 (96%) were positive for one or both of these carcinogen metabolites. NNAL or NNAL-Gluc was also detected in 10 of 20 samples (50%) in which total cotinine was < 5 ng/ml. The more frequent detection of NNAL and NNAL-Gluc than of total cotinine may be due to pharmacokinetic differences of these metabolites. In this study, NNAL plus NNAL-Gluc correlated with total cotinine ($r = 0.71$; $p < 0.0001$). Concentrations of NNAL, NNAL-Gluc and total cotinine are shown in Table V-17 below. Concentrations of cotinine, NNAL, and NNAL-Gluc were not significantly different in samples collected twice from the same children at 3-month intervals. Authors noted that levels of NNAL plus NNAL-Gluc were comparable to those they observed in previous studies of adults exposed to ETS. Authors also noted that while it is likely that uptake of nicotine and NNK by the children in this study was attributable to ETS, it is possible that some of the children may have smoked a cigarette.

Table V-17

Concentrations of NNAL, NNAL-Gluc, and Total Cotinine (mean ± SD) in the Urine of Elementary School-aged Children[1]

Group	No. of children[2]	NNAL (pmol/ml)	NNAL-Gluc (pmol/ml)	NNAL + NNAL-Gluc (pmol/ml)	Total cotinine (ng/ml)
All	74	0.081 (± 0.030)	0.040 (± 0.050)	0.056 (± 0.076)	12.0 (± 17.8)
ETS exposure reported in questionnaire	38	0.032 (± 0.039)	0.064 (± 0.056)	0.095 (± 0.088)	24.5 (± 22.4)
No ETS exposure reported in questionnaire	35	0.010 (± 0.020)	0.026 (± 0.040)	0.035 (± 0.058)	5.0 (± 8.7)
Total cotinine[3] < 5 ng/ml	20	0.005 (± 0.010)	0.012 (± 0.020)	0.016 (± 0.030)	1.2 (± 1.6)

[1]Source: Hecht *et al.*, 2001.
[2]One child did not have questionnaire data on exposure.
[3]Total cotinine < 5 ng/ml is the cutoff used by the authors to indicate ETS exposure.

Nafstad et al. (1996) examined the relationship between maternal smoking habits and concentrations of thiocyanate and cotinine in cord blood. (The results regarding cotinine are summarized above.) The women in this study were self-reported non-smokers, occasional smokers, and daily smokers. Among newborns of mothers smoking 1-9 cigarettes per day, the median concentration of thiocyanate was 43 μmols/L (25-75th percentile: 23-58 μmol/L) and among newborns of mothers smoking 10 or more cigarettes per day the median thiocyanate concentration was 62 μmols/L (25-75th percentile: 44-71 μmol/L). The correlation between the average number of cigarettes smoked by the mothers and the concentration of thiocyanate in cord serum was 0.46 ($p=0.003$), and the correlation between thiocyanate and cotinine was 0.63 ($p<0.001$). Using linear regression analysis of just the daily smokers, the increase in the concentration of thiocyanate in cord serum per daily cigarette smoked was 2.3 μmol/L.

In a study by Tang *et al.* (1999), 4 biological markers of ETS exposure were evaluated in a cohort of Hispanic and African-American preschool children. There were 109 children included in this study, from 1 to 6 years old. Investigators measured plasma cotinine, protein adducts of 2 carcinogens (*i.e.*, the hemoglobin adducts of 4-aminobiphenyl (4-ABP-Hb) and the albumin adducts of polycyclic aromatic

hydrocarbons (PAH-albumin), and sister chromatid exchanges (SCEs; used as a general indicator of genetic damage). Information on ETS exposure at home was obtained by questionnaire. All of the biomarkers were higher in ETS-exposed children than in unexposed children. The differences were statistically significant for cotinine ($p < 0.001$), 4-ABP-Hg ($p < 0.05$) and PAH-albumin ($p < 0.05$). SCEs were marginally higher ($p = 0.076$). In addition, when children were grouped by exposure (no reported ETS exposure, exposure by household members other than the mother, or exposure from maternal smoking) all of the biomarkers increased across exposure groups, although the differences were not always statistically significant. And finally, African-American children had higher levels of cotinine ($p = 0.059$) and PAH-albumin ($p = 0.02$) than Hispanic children, after adjusting for exposure. Authors note that this finding is limited by small numbers and the possibility of exposure misclassification; however, it is consistent with other data showing ethnic variation in the internal dose of ETS observed in adults. It is also consistent with the results observed in children in the analysis by Mannino *et al.* (2001), as previously discussed.

9. Summary and Conclusions

Cotinine, the major metabolite of nicotine, has emerged over the past 20 years as the biomarker of choice for most field exposure studies and for validation of smoking status. Physiologic cotinine concentrations differ typically by several orders of magnitude between smokers and ETS-exposed non-smokers. Cotinine is a sensitive enough biomarker that its concentrations can reliably distinguish between non-ETS-exposed persons and ETS exposed non-smokers with low, moderate and high levels of exposure. However, due to a half-life of around 20 hours, cotinine levels in body fluids reflect exposures only during the preceding day or two. To the extent that these exposures are typical, cotinine levels are a good measure of an individual's general ETS exposure. However, when exposures are episodic or characteristic of a particular environment (e.g. work vs. home), the timing of sampling is critical to avoid over- or under-estimation of exposure. Sampling at multiple, varied times, and/or measurement of tissues reflecting longer-term exposures, such as hair, are useful in this context. Future data may show that the relationship between ETS exposure and cotinine levels are potentially strong enough to link adverse health outcomes to physiologic cotinine levels. These same data may be useful in determining which study subjects may actually be smokers rather than ETS-exposed non-smokers that would otherwise skew study findings. Results from ongoing personal exposure monitoring studies are shedding light on the relationship between inhaled nicotine concentrations and physiologic cotinine concentrations. These studies also show that there is a relationship between the relative contributions to ETS exposure in the home and workplace with the smoking activity found in those environments.

Hair nicotine is an emerging biomarker that may be as effective as cotinine in determining levels of ETS exposure. Hair nicotine has the important advantage of providing an integrated measure of exposure over a period of months. As such, it is less susceptible to measurement errors associated with the timing of sample collection, as may occur with cotinine measurements in body fluids in cases of episodic versus continuous passive exposure. However, relatively few studies have used hair nicotine

as a biomarker for ETS. Larger studies are needed to determine the effects of hair color and hair treatments on nicotine binding, and show that hair nicotine is a viable biomarker for ETS.

Another tobacco-specific biomarker with good ability to differentiate among smokers, non-smokers with ETS exposure, and those without, is NNAL. This metabolite of the carcinogen, NNK, has been detected in several body fluids in association with tobacco exposure. Assayed in conjunction with its glucuronide conjugate, it is an especially attractive compound for analyses of urine. However, it has thus far not been widely applied in studies of passive smoking.

Other biomarkers of ETS exposure, such as DNA and protein adducts, link ETS exposure directly to carcinogenic metabolites. These biomarkers, while useful in linking tobacco smoke exposure to toxic or carcinogenic end points, are generally not used to distinguish between ETS-exposed non-smokers and unexposed non-smokers. The use of carbon monoxide and thiocyanate as ETS biomarkers are not specific to tobacco smoke and therefore have limitations for use as biomarkers. Cotinine, nicotine, and NNAL/NNAL-Gluc are the only biomarkers that have been demonstrated to be both tobacco-smoke specific and able to reliably distinguish between ETS exposed and unexposed non-smokers. Of these, the assays for cotinine have been the best developed and most widely applied. For this reason, cotinine is currently the preferred biomarker for comparison among studies of ETS exposure. When attempting to quantify degrees of ETS exposure, the other biomarkers discussed in this chapter are of less utility.

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